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CONTENTS.

	PAGE
Narcosis. By Dr. Max Verworn	97
A Brief Notice of Felix Platter, with Extracts from his MS. Memoirs Preserved at the Library of Bâle. (Illustrated.) By Charles Greene Cumston, M. D.	105
Tuberculosis in Infancy and Childhood. By Henry Koplik, M. D.	113
The Effect of the Prevention of Laking on the Catalytic Activity of the Blood. By Abraham Strauss	120
Pin Worm Appendicitis. By Grover C. Ney, M. D.	123
Notes on New Books	125
Books Received.	126

NARCOSIS.*

By Dr. Max Verworn,

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Mr. President, Ladies and Gentlemen:

Two main reasons induced me to select the subject of narcosis for my lecture before your society. On the one hand, I am following herein the suggestion of your honored president; on the other hand, the problem of narcosis has a personal attraction for me, since I and my colleagues at Göttingen, as well as in Bonn, have devoted a great deal of attention to its investigation. Furthermore, I believe that this theme, the subject of narcosis, possesses an especial interest for medical men, not only from the theoretical but also from the practical side. From the theoretical side, because the processes of narcosis introduce us into the most profound secrets of the mechanism of living matter; from the practical side, because it is incumbent upon the physician to know the actual nature of the condition, which he so often induces in man. Practical and theoretical interest have here, once more, the same object. Such union of practical and theoretical interests makes our medical work so fruitful and lends it a special charm among the biological sciences. This is especially manifest in the study of the peculiar phenomena of narcosis, and is also the reason why the subject of narcosis has been so extensively investigated, especially in the last decades.

* Lecture delivered before the Harvey Society in New York, October 28, 1911, and before the Johns Hopkins Hospital Medical Society, October 31, 1911. The secretary of the Harvey Society has kindly granted us permission to publish this paper in advance of its appearance in the proceedings of the Harvey Society.

The knowledge of the use of narcotic substances, especially those from the vegetable kingdom, is ancient. It extends back to prehistoric times, as we may deduce by analogy with primitive races living to-day. Man has been, from the first, a student of nature. He was forced to adapt himself, at every step, to his environment. This he could do only by very close observation of nature, for there was danger lurking for him wherever, in his wanderings, he was confronted with new conditions. Thus, in his quest for food he had to learn to recognize the peculiar poisonous effects of plants. All primitive races are familiar with them and employ them for various purposes. The use of narcotizing substances, especially for purposes of enchantment, was well-known in the Homeric age. Circe mixed narcotic juices with the food of the companions of Odysseus, making them forget their homes; and Hermes knew already an antidote, which he gave to Odysseus as a protection: *μῶλυ δὲ μὶν καλέουσι θεοί.* In Homer we also find, for the first time, although not in connection with poisonous action, the word from which the modern term "narcosis" is derived. The verb *ναρκάω*, "I am paralyzed," appears in Homer as *ἄπαξ εἰρημένον*, when he describes how Hector struck Teukros on the shoulder with a sharp stone, so that his hand, paralyzed, let fall the bow (Iliad VIII, 328). This venerable word serves us to-day to distinguish a special group of paralyses, or depressions, which are induced by chemical substances.

The scientific study of narcosis begins, however, only with the time when narcotics came into general use in medical practice for the relief of pain, especially since, in Boston, in 1846, the chemist Jackson and the dentist Morton introduced ether into surgical practice. Soon after this momentous event experiments began for the purpose of explaining the striking action of anesthetics. Among the numerous explanatory efforts, however, there are only two series of attempts which deserve scientific consideration.

In one series, it has been tried to establish a relation between the depressing action of narcotics and their solubility in certain constituents of the organism. As early as 1847, Bibra and Harless used the fact that cerebral fats are readily soluble in such narcotics as ether and chloroform, as a basis for a hypothesis of the mode of action of narcotics. They assumed that the narcotics act as anesthetics by extracting the brain-fats. Hermann indicated later a similar conception, and recently Reicher has shown that in deep and long-continued narcosis the fat-content of the blood rises indeed quite markedly. While already in these assumptions the relations of solubility between fats and narcotics stand in the foreground, Richet has later on called attention to a second relation in regard to solubility. He noticed that many narcotics were distinguished by a very low degree of solubility in water, and believed that, on the basis of his observations, he could make the general statement that a substance acts the more strongly as a narcotic, the less it is soluble in water. The relations between the solubility of narcotics in fats and water and their depressing action, which in the before-mentioned observations and hypotheses were expressed so incompletely and obscurely, were first made clear and formulated according to definite laws by Overton and by Meyer, independently of one another. Hans Meyer and Overton were able to show that the intensity of the narcotic action of any substance is dependent on the proportion in which it is distributed between water and fat when it is shaken with a mixture of fat and water. The coefficient of distribution, that is, the proportion of solubility of the substance between water and fat, is the greater, the stronger its narcotic action. That is to say, a substance acts the more strongly as a narcotic, the more soluble it is in fats and lipoids and the less soluble it is in water. Meyer and Overton have confirmed this law on a very large number of narcotics. This interesting fact contains apparently a very important requirement for the production of narcotics, although it does not present a "theory of narcotics," as has often been incorrectly stated. It shows us one factor that must be realized if the narcotic is to reach its field of action, but it tells us nothing concerning the mechanism of the narcotizing action itself.

The second series of explanatory attempts ascribes the depressing action in narcosis to a change in the state of aggregation of certain components of the protoplasm under the influence of the narcotic. Claude Bernard, who noticed the rigidity of muscles which is produced by the influence of chloroform vapor or heat, was the first one to express the view that narcosis consists in a "semi-coagulation" of the protoplasm. Binz came to the same conclusion from a microscopic study of ganglion cells and unicellular organisms. He found that the protoplasm of the cells became opaque, granular and dark under the influence of the narcotic, as is the case in coagulation, and he sees therefore, in narcosis, a depression by coagulation. As a matter of fact, it is easy to observe such changes in unicellular organisms under the influence of large doses of narcotics, but recovery from such a state is no longer possible. In recent times, Höber has expressed similar opinions. Höber makes the hypothesis that the process of excitation is associated with a loosening of the protoplasmic colloids, which consist of lipoids and proteids. In connection with this assumption, Höber offers the further hypothesis that narcotics inhibit this loosening of the colloids, especially in the superficial protoplasmic layers of the cell, so that in consequence the irritability is reduced or abolished.

Thus, we see that widely different hypotheses concerning the nature of narcosis have been expressed, without any of them having as yet achieved general acceptance.

Before we attempt to form a conception of the mechanism of narcosis, it appears to me indispensable that we clearly understand what should be required of any theory of narcosis. Narcosis is a state of living matter, in which, under the influence of certain chemical substances, the physiological processes of the cell are altered in a special way. A scientific study of this state can only consist in seeking to determine, as far as possible, the nature of these changes. The more deeply we analyze them, the clearer becomes the theory of narcosis. In order, however, to comprehend the changes in the physiological processes in living matter, it is requisite that we should first know the normal physiological processes themselves, in all their details. In spite of many important and fundamental researches, we are to-day still far from such knowledge. From this it is evident that we cannot yet speak of a "final" theory of narcosis. But where in our knowledge do we arrive at final results? Wherever we may look, whatever we may achieve, we are always and again confronted with new problems. Is there, anyway, a finality anywhere? Whoever, impatiently rushing forward, looks for a final word in knowledge will, like Goethe's Faust, only experience grievous disappointment:

> "Entbehren sollst Du, sollst entbehren!
> Das ist der ewige Gesang,
> Der jedem an die Ohren klingt,
> Den unser ganzes Leben lang
> Uns heiser jede Stunde singt."

On the other hand, whoever is conscious that all things stand in endless coherence will desist from seeking an imaginary goal, and instead will enjoy the inexpressible charm which lies in the unlimited possibilities of finding again and again new links of this coherence The possibilities of knowledge are endless, because the world is endless. This is true in large as well as in small things, and is true also of our problem. To the extent to which we succeed in discovering new facts which characterize the state of narcosis, to that extent the theory of narcosis develops of itself.

Well, then, what do we know of the changes which living

matter undergoes during narcosis? Narcosis is a state of depression. Let us understand what this means. All states of depression in living systems are characterized by the fact that all or single partial processes of the normal metabolism undergo a retardation of their course, which may amount to complete standstill. This shows itself in the following symptom-complex. The specific manifestations of life of that system are depressed or extinguished. The irritability to external stimuli is lowered, so that stimuli which are effective in the normal state, show no apparent result. At the same time the power of conductivity, that is, the transmission of the excitation from the point of stimulation to some distant place, is correspondingly restricted, for irritability and conductivity run always and everywhere along parallel lines. This symptom-complex occurs in the most diverse living systems and under the influence of manifold agencies. We see it as a result of low temperatures in "frigor depression," or as a result of high temperatures in "heat depression"; we meet it after extreme functional activity as fatigue; after withdrawal of oxygen, as suffocation; under the influence of chemical substances, as toxic depression; after too low osmotic pressures of the surrounding medium, as "water rigor"; from stoppage of the blood-supply to the tissue cells, as asphyxial depression; and under many other conditions.

The question now arises, whether the mechanism of the depressing process is the same under all these widely diverse circumstances. In its generality, we can at once answer this question in the negative. The mechanism of depression in water rigor and in acid-intoxication, for instance, is entirely different. Nevertheless, comparative studies of the mechanism of depression under the influence of different factors have shown me that a particular tendency exists toward one etiologic type of depression. In the complex realm of metabolism in all aërobic forms of cell, one part of the many anabolic and catabolic processes is especially sensitive to external influences, and that is the oxygen metabolism. Here is, in a certain sense, the *locus minoris resistentiæ* of the living matter of all aërobic organisms. In fatigue, it is the relative deficiency of oxygen which produces the depression. The increased demand for oxygen, brought about by the increased functional activity, can no longer be satisfied by the amount of oxygen present. The same is true of heat depression. The supply of oxygen cannot keep pace with the accelerated catabolism of the living tissue, induced by the temperature. In the asphyxial depression of the tissue cells which occurs as a result of any stoppage of the blood-supply, it is not the withdrawal of the organic nutritive materials in the blood, but only the lack of oxygen, which produces the depression. In prussic-acid poisoning, again, it is the suppression of the oxygen metabolism in the tissue cells which produces death. Thus we see that oxygenation is the factor, in the metabolism of aërobic cells, which most easily fails under diverse external influences and so forms the starting-point for the development of depression.

The most simple paradigm of this entire group of depressions is therefore suffocation of living cells or tissues in indifferent media free of oxygen. Fortunately we know to a certain extent the working of the mechanism of suffocation.

In normal metabolism during rest the supply of oxygen is always sufficient for the needs of the cells. Molecular oxygen is absorbed by them from the surrounding medium. A certain reserve supply of molecular oxygen, although comparatively small, is always present in the cells themselves, at least in cold-blooded animals not kept at too high a temperature. Many facts force us to this opinion, especially the continuance of normal production of energy and of irritability for a longer or shorter time, under complete exclusion of oxygen supply. The oxygen taken up from the medium is activated by special oxygen-carriers and distributed to the oxidizable substances. We know of the existence of such oxygen-carriers in the most diverse animal and vegetable cells, and we are accustomed to group them together under the collective name of "oxydases," although their chemical constitution is still completely unknown. The oxygen-carriers bring activated oxygen, in the manner of inorganic catalysators, to the oxidizable substances, which by the oxidation are split into carbon dioxide and water. One point here remains still undecided, and that is, whether the oxidation attacks the organic fuel directly, such as, for instance, the carbohydrates, which have been synthetically built up by anabolic processes, or whether only the fragments are oxidized to carbon dioxide and water, while the splitting itself is accomplished by enzymatic processes. It is possible that in different forms of living substances the catabolism takes a different course. At any rate, the principal source of energy in all aërobic organisms is to be found in the oxidative splitting-up processes, and not in the non-oxidative part of the catabolism. These oxidative splitting-up processes represent the principal source of energy-production. That is an important fact. It has a special bearing upon the degree of irritability of living matter, for irritability is measured by the amount of energy-production which results from a stimulus.

What changes does this phase of metabolism undergo, when the external supply of oxygen is withdrawn from a living system? No more molecular oxygen enters the living matter from the outside. The molecular oxygen, which at the moment of exclusion of oxygen is still present in the living tissue, will, according to its amount, be used up sooner or later. In the same proportion the extent of the oxidative breakdown will decrease. The catabolism will occur more and more in a non-oxidative manner. As soon as all the oxygen is used up, the destructive process will be entirely non-oxidative. This gradual transition from oxidative to exclusively non-oxidative decomposition corresponds in a characteristic way to the development of the depression. The intensity of the spontaneous vital activities diminishes gradually after the interruption of the external supply of oxygen. Very gradually the irritability for external stimuli decreases. Very gradually also the extension of the excitation from the point of stimulation to adjacent parts becomes restricted. Finally no spontaneous manifestations of life are visible; finally no visible effect

is to be obtained from the strongest external stimuli. These are the general consequences which result from an interruption of the oxygen supply and which we observe everywhere in whatever way and at whatever point the oxygen metabolism is disturbed.

I have dwelt in some detail on the relations of the metabolism of oxygen and its disturbances, because our investigations carried out in the laboratories at Göttingen and Bonn have shown that in narcosis, also, there is a similar interference with the oxidation process. The fact that the oxygen metabolism suffers readily under diverse external influences, suggested the question whether also, under the influence of narcotics, disturbances of the oxidative processes take place. I had previously studied, by means of an artificial circulation, the rôle of oxygen metabolism in fatigue of the spinal cord of the frog, made especially sensitive by mild strychnin poisoning. It seemed to me, from my experience, that this would be a favorable object for the experimental determination of the question whether the oxidative processes are interfered with during narcosis. This question could be particularly well studied on the fatigued spinal cord, because it was found that the fatigue can be completely removed again only by the supply of oxygen. If the spinal cord is fatigued and oxygen is not supplied, as can easily be done with an artificial circulation, and if now the completely fatigued and oxygen-greedy spinal cord is narcotized, it can be determined whether, with a free supply of oxygen, the spinal cord can take it up, and thus recover during narcosis. If the fatigued cord is irrigated during narcosis with arterial ox blood or with an oxygen containing saline solution, and later, while the narcosis still continues, the blood is removed again by oxygen-free salt solution, and if then the narcosis is stopped, it must become manifest whether the centers of the cord have taken up the abundantly supplied oxygen during narcosis, and recovered. Winterstein has performed this experiment at Göttingen, using various narcotics, such as ether, alcohol, chloroform and carbon dioxide. All the experiments agreed in showing that not the least trace of recuperation occurred; while, after the end of the experiment, the cord was completely restored in a few minutes by perfusion with oxygenated ox blood without narcosis. Herewith the first proof was given that, during narcosis, living tissues are unable to utilize the oxygen offered to them.

Nerves offered a second favorable object for testing our question. We had succeeded, after many vain attempts, in perfecting a method by which it was possible to show that nerves died of suffocation when cut off from all possible supply of oxygen. This fact, established by H. von Baeyer, placed us in a position to make on the nerve, which proved to be an exceedingly favorable object, experiments on the question of oxygen metabolism during narcosis analogous to those made on the cord. The sciatic nerve of the frog was asphyxiated, and thus made oxygen-greedy. When its conductivity was lost and its irritability reduced to a very low level, it was narcotized with ether. Then, during narcosis, oxygen was supplied to it for a long time. After the oxygen had been finally removed by pure nitrogen, the narcosis was stopped. In these experiments, which were first made by myself, afterwards by Fröhlich, and later on by Heaton, there was never any trace of recovery. When the nitrogen was replaced by air, the nerve recovered in one minute and showed normal irritability and restoration of conductivity.

Finally, in a series of experiments which have not yet been published, Ischikawa proved that amœbæ, also, which have been asphyxiated in a gas-chamber in pure nitrogen and have become motionless, did not take up oxygen which was supplied to them during narcosis, while after stopping the narcosis and replacing nitrogen by air they rapidly resumed their amœboid motion.

These experiments show unequivocally *that living tissues, even when their demand for oxygen has been raised to an extreme degree by fatigue or asphyxia, cannot, during narcosis, make use of oxygen, even when offered to them abundantly.*

This conclusion caused us to advance one step further. If living tissue, during narcosis, cannot use the oxygen which is supplied to it, this inability might be produced in several ways. Either narcosis depresses the entire phase of catabolism, with all its partial processes, perhaps by paralyzing the first step, or it hinders especially only the oxidation processes. In the former case, we should expect that a narcosis of a certain depth, in which the destructive processes were completely abrogated, could continue for an indefinite time. In the second alternative, that is, if only the oxidation is prevented, destruction must proceed in non-oxidative form, just as in the absence of external oxygen supply, and the living tissue under narcosis must eventually die of asphyxia, even though sufficient oxygen is constantly at its disposal. We can decide between these two possibilities. On the one hand, experience shows that no narcosis, whatever its depth, can continue indefinitely without the tissue losing its viability. On the other hand, we can demonstrate experimentally that during narcosis catabolism proceeds in non-oxidative manner and that asphyxia gradually supervenes. Here again the nerve proved to be a favorable object for experiment. Heaton has used the two sciatic nerves of the same frog for the following parallel experiment: One nerve was drawn through a gas-chamber which contained pure nitrogen; the other was narcotized in a similar gas-chamber filled with air. The experiments began simultaneously in the two nerves. In the asphyxiated nerve the irritability sank very gradually lower and lower. When it had fallen to a certain level, the conductivity for an excitation coming from the part of the nerve outside of the gas-chamber vanished also. The time at which this degree of depression is reached depends on the length of the asphyxiated portion of the nerve, on the condition of the frog, and on the temperature. At room temperature it requires, on the average, from two to three hours. At the time that the conductivity of the asphyxiated nerve was abolished, the air surrounding the narcotized nerve was replaced by pure nitrogen, and the narcosis interrupted, so that the nerve, after the narcosis was

stopped, had no more oxygen at its disposal. If the whole destructive phase of metabolism had been brought to a stop, the nerve should, after stopping the narcosis, be in about the same condition as before it. This was, however, not the case. All the experiments, rather, agreed that during narcosis this nerve was also asphyxiated like the nerve in pure nitrogen, in spite of the fact that the former always had air at its disposal. Its irritability had been greatly reduced and its conductivity was abolished. That it was actually asphyxiated was shown by the control experiment, in which both nerves recovered completely as soon as air was conducted over them. The irritability increased rapidly and the conductivity returned.

Ischikawa has recently performed similar experiments on amœbæ. Amœbæ gradually lose, in nitrogen, their amœboid motions. They regain them only when oxygen is supplied. If amœbæ are narcotized with ether, they are also asphyxiated; for after the narcosis, in the absence of oxygen, they do not regain their amœboid motions. These only return after oxygen is supplied.

It is thus evident that living tissue is asphyxiated during narcosis; that is, that the destructive phase of metabolism proceeds in a non-oxidative manner.

We can add yet another fact. Even during narcosis *the destructive processes can be increased, that is, accelerated, by exciting stimuli.* Heaton has narcotized the two sciatic nerves of a frog in a double chamber under absolutely identical conditions. While one of them remained at rest, the other was continually stimulated by a faradic current applied to the end beyond the chamber. After discontinuing the narcosis in pure nitrogen it was always found that the irritability of the stimulated nerve had fallen to a lower level than that of the other. Placed in air, both recovered to an equal degree. The results of this experiment entirely agree with the phenomena of fatigue, which were found by Thörner in his researches on the fatigue of nerves in nitrogen. On the basis of all these experiments, we may make the following statement: *Living tissue becomes asphyxiated during narcosis. The catabolic phase of metabolism continues in the form of a non-oxidative destruction, just as in asphyxia, and can also, as in asphyxia, be accelerated by exciting stimuli. Recovery from this asphyxia is, as in every asphyxia, only to be attained by supplying oxygen.*

Under these circumstances the idea naturally presents itself, that the entire symptom-complex of narcosis is only a manifestation of asphyxia, which the narcotic induces by inhibition of the oxidative processes. Before we accept this idea, however, we must assure ourselves that there is no fact which stands in the way of its acceptance. It goes without saying, that if asphyxia occurs in narcosis, the general picture of asphyxia must be present. This is actually the case. The cessation of spontaneous evidences of life, the reduction of irritability, the decreased power of conductivity—all the typical symptoms are identical in narcosis and in asphyxia in an oxygen-free medium. In only one point is there a noteworthy difference. *That is in the time relations of the depression-symptoms.* In narcosis of nerves, for instance, irritability sinks *in a few minutes* to a point which in pure nitrogen is only reached in *two or three hours.* The question therefore arises, whether we have not here a fact which must inevitably eliminate the idea that narcosis is nothing more than asphyxia. A more careful consideration shows, however, that this is not the case. The experiments which have already been described contain the explanation of this difference in the rapidity of onset of the depression.

The fact that living cells, during narcosis, can make no use of molecular oxygen, even when it is freely offered to them, shows that the narcotic renders the living tissue incapable of undergoing oxidations. It cannot, therefore, utilize for its oxidation processes the oxygen present in itself. The conditions during asphyxia in an oxygen-free medium are, however, quite different, as for instance in asphyxia of nerves in nitrogen. Here the power to carry on oxidations is not interfered with in the least. As long as any trace of molecular oxygen is present, it can be used for oxidation. Now it is of course impossible that, at the moment that the air in a gas-chamber is replaced by nitrogen, every trace of oxygen should disappear from the nerve in the chamber. The nerve, therefore, with its small oxygen requirement, can, even in pure nitrogen, carry on its oxidation processes in a more or less decreasing degree, according to the temperature and to the amount of oxygen contained in the nerve itself. Accordingly, the irritability decreases only gradually, and in proportion to the extent of the decrease of the oxidative processes. *In the depression of nerves in an oxygen-free medium we deal with a slow, while in narcosis we deal with an acute, asphyxia.* That is the factor which produces the difference in time. We have also, therefore, the power of eliminating this difference completely. We may do this, in one way, by those measures which hasten asphyxia in an oxygen-free medium. Such a measure is the increase of the demand for oxygen by raising the temperature. In this case heat depression occurs. Of heat depression we know that it is an asphyxia which results from a relative lack of oxygen, because the supply of oxygen cannot keep pace with the markedly increased demands of the living tissue, just as in fatigue. As H. von Baeyer has shown, complete loss of irritability in nerves may be attained by keeping them for 20 minutes in a gas-chamber at a temperature of 42° to 47° C. The lost irritability cannot be restored by reduction of temperature alone; while, after supplying the nerve with fresh air, recovery results in a few minutes. At higher temperatures asphyxia occurs still more rapidly. In the ganglion cells of the cerebral cortex of mammals, asphyxia results in a few seconds when the air supply is cut off. On the other hand, the narcosis of the nerves can be greatly delayed if the narcotic is administered only in small amounts. In short, *the more rapid or slower onset of depression is solely dependent on the rapidity with which the oxidation processes are abolished.* In narcosis this occurs very rapidly, because the narcotic renders the cells incapable of carrying on oxida-

tions; in asphyxia in oxygen-free media, it occurs only very slowly, because the living tissue retains its power to carry on oxidation and continues to do so until the last trace of oxygen present in the tissues is used up. The difference in the time of development of the depression in the two cases is solely dependent on the different way in which the oxidation processes are brought to a standstill. The symptom-complex of narcosis, therefore, not only is comprehensible, but on the basis of the ascertaind facts it is a requirement.

It seems to me that, after these considerations, it is no longer possible to doubt, not only that narcosis is accompanied by asphyxia, but that the acute asphyxia is the deciding factor which produces the depression. This does not exclude the possibility that the narcotic may also produce other changes in the living matter, for instance changes in the state of aggregation of certain substances. Whatever other changes may occur, *the factor which produces the characteristic symptom-complex of narcosis is under all circumstances the suppression of the power to carry on oxidations.*

The conclusions which may be drawn directly from the facts bring us this far; but the problems are by no means finished. At this juncture the new question arises: In what way does the narcotic, by entering the cell, inhibit the power of the latter to carry on oxidations? Here the facts leave us still in the dark. If we wish to answer this question, it can only be done in the form of a hypothesis. I wish to emphasize this point particularly. But *"no true scientist fails to realize that the essential factor of progress lies in a hypothesis which agrees with the facts."* These words of one of the greatest physiologists, who was also my predecessor in Bonn, shall serve as my excuse if I attempt now, with the assistance of a working hypothesis, to go a step further in the direction indicated.

When we recall the fate of molecular oxygen in the normal metabolism of the cells, from the moment at which it enters the living substance to the moment at which it decomposes the oxidizable materials into carbon dioxide and water, we find that the narcotic, which overflows the cell, could establish its inhibitory action upon the oxidation at various stages of this process.

In the first place we might conceive *that the narcotic, when it has penetrated into the living substance, prevents in some way the entrance of molecular oxygen from the surrounding medium into the cell.* This assumption, however, may be dismissed at once. If the depression of narcosis were produced by the fact that oxygen could not penetrate into the cells, then we could expect a course of depression with exactly the same time relations as in complete withdrawal of external oxygen; the cell would be in exactly the same position as it is, for instance, in pure nitrogen. The difference in the time relations between the two cases, for instance in the nerves, shows us, however, that this is not the case.

Next we must consider the possibility *that narcotics appropriate the oxygen which enters the cells, and use it for their own oxidation.* The narcotics are, it is true, generally looked upon as chemically indifferent substances, but Bürker has recently published experiments which show that, under certain conditions, narcotics may be oxidized, at least by nascent oxygen. Bürker performed the following interesting experiment. He placed two identical voltameters in the same electric circuit. One of them was filled with acidulated water; the other had in addition a small percentage of ether. Then he decomposed the fluids electrolytically by means of a galvanic current. In the voltameter which contained no ether, the gas collected at the two poles in the usual relation, the volume of hydrogen at the cathode being to the volume of oxygen at the anode as 2 to 1. The relationship was, however, entirely different in the voltameter which contained ether. Here only a very small amount of oxygen collected at the anode; while the analysis of the gas from the anode showed that carbon dioxide, acetaldehyde and acetic acid had also been formed, as oxidation products of ether. Based on this result, Bürker put forward the hypothesis that narcotics had the same effect in living substance as in the voltameter, and that the depression of the oxidation process in narcosis depends on the fact that the narcotic itself appropriates the oxygen. As, in living tissue, oxygen is activated by oxygen-carriers, the possibility of oxidation of ether even in the cells is not, indeed, excluded. But under the conditions which obtain in living tissue, it is doubtful whether it really occurs to such a degree as to reduce the oxidation of respiratory materials to a noticeable extent. For many of the narcotics, oxidation in the cells is very unlikely, and in the case of carbon dioxide it is absolutely excluded.

A third possibility of the interference with oxidation is, *that the narcotic in some way blocks the molecules of oxidizable material, perhaps by a loose chemical fixation, and thus renders them inaccessible to oxidation,* and the oxidation will thus cease. However, this view also has very little likelihood. According to this view, we would have to presuppose that the narcotics, which in themselves present substances with very heterogeneous chemical properties, were also able to block very diversified substances; for in non-oxidative catabolism, such as occurs in narcosis, manifold products arise with very different chemical properties. We would have to assume that all these different substances can be prevented from oxidation by all the different narcotics. We cannot readily have recourse to such an assumption.

Finally, there remains one more possibility to be considered. It might be assumed *that the narcotic renders the oxygen-carriers incapable of activating the oxygen, so that the oxidizable materials could no longer be oxidized and decomposition would proceed only in non-oxidative form.* This view seems to me the most probable, as we have inorganic analogies for it. The colloidal solutions of metals, for instance platinum solution, can, as Bredig has shown, be prevented from acting as oxygen-carriers by diverse chemical substances, such as corrosive sublimate, hydrogen sulphide, hydrocyanic acid, etc. "Paralyses," or depressions, are produced in this way, which correspond to a great extent with the depressions of living

cells. If I therefore form the hypothesis that narcotics, in an analogous way, render the oxygen-carriers in living tissues incapable of carrying oxygen, all the facts of narcosis find a simple mechanical explanation.

But still more; the possibility is also given, here, to combine the relation between the solubility in lipoids and narcotic action, discovered by Overton and Meyer, with the facts already given concerning the influence of narcotics on oxidation processes. The fact that the lipoid solubility of a substance primarily determines the degree of its narcotic action, shows us that the mechanism which lies at the base of the symptom-complex of narcosis must be associated in some way with lipoids. We have seen that this mechanism consists in an inhibition of oxidations, and it is highly probable that this comes about through a paralysis of the oxygen-carriers. It is quite natural to assume that the oxygen-carriers, whose chemical nature is still entirely unknown to us, stand in some close relation to the lipoids, that they are perhaps themselves of lipoid nature, or that they are attached as specific atom groups to lipoid molecules. By this assumption the relations discovered by Hans Meyer and Overton and the facts shown by us, that narcosis depends on acute asphyxia, would be combined in a natural manner. Both facts would mutually complete each other, and the result would be a further elucidation of the mechanism of narcosis.

However, I wish to emphasize, again, that the conception regarding the nature of inhibition of oxygen metabolism in narcosis is of a purely hypothetical character. It is only an established fact *that narcotics induce an acute asphyxia of the cells. Herein is the essence of narcosis.*

If we are satisfied, for the present, with this knowledge and leave the question of the particular mechanism of the asphyxia to one side, the mere fact that narcotics inhibit oxidation processes will in itself guard us from many false conceptions in regard to narcosis. The knowledge of this fact has some significance also for the practical use of narcosis.

Let us ask, first, what we narcotize when we induce narcosis in man by inhalation of ether or chloroform. All tissues of the body are not affected equally by any means. Even if it is assumed that the blood carries the narcotic to all the tissues in nearly the same concentration, the different tissues are influenced to a very different extent by the narcotic. When the ganglion cells are already completely depressed, the nerve-fibers and muscles still show no sign of narcosis. The ganglion cells of the brain, and especially those of the cerebral cortex, are most readily affected in their specific functions by narcotics. Thus, if we induce so-called "general" anesthesia by ether or chloroform narcosis for any operative purpose, we deal in reality only with narcosis of the cerebral cortex. In this lies the great value of narcosis; for we desire in narcosis to eliminate conscious sensation, and the acts of consciousness are, as is well-known, due to excitation of the ganglion cells of the cerebral cortex. The ganglion cells of the cerebral cortex, with their functions intact, are the most valuable asset that man possesses. Therefore it is particularly important to us that nothing shall happen which might injure them permanently, and we must therefore know the possible dangers of narcosis, in order to avoid them.

The fact that the ganglion cells of the cerebral cortex lose their specific functional activity, under the influence of narcotics, sooner than any other body cells, must, on the basis of our new data in regard to the relationship of narcosis and asphyxia, naturally give rise to the idea that they are more sensitive to asphyxia than any other body cells. That is actually the fact to a striking extent. Mosso has demonstrated this in a classic way on man, in whom alone direct studies of the conditions of the processes of consciousness can be made. In his experiments on Bertino, he found that a few seconds interruption of the supply of oxygen sufficed to produce loss of consciousness. Bertino had a large defect in his skull over the frontal lobe, and the cerebral pulsation could be graphically recorded there. The frontal lobe receives its blood supply from branches of the carotid arteries. When Mosso compressed these arteries in the neck, so that the cerebral pulsation ceased, Bertino lost consciousness in five seconds without having had any premonitory disagreeable sensations. After releasing the pressure upon the carotid arteries, consciousness returned at once. This experiment shows how dependent the cells of the cerebral cortex are on their supply of oxygen, and in how short a time unconsciousness occurs after complete interruption of this supply. Here we have an example of a depression rapidly following the withdrawal of oxygen. The associative workings of our ideas and sensations, thoughts and feelings can proceed in an undisturbed manner only when there is complete integrity of the specific irritability of all the ganglion cells concerned. The slightest loss of irritability interrupts the orderly play of excitations and inhibits the activity of consciousness.

From this peculiarity of the cortical cells is the important requirement derived, long known empirically, that in man we should employ a light degree of narcosis, just sufficient to paralyze consciousness. Under such circumstances the depression of the oxidative processes is undoubtedly of very limited extent, and there is no demonstrable danger of permanent injury to the normal brain. When we employ a deeper narcosis, the danger of rapid and complete asphyxia of the ganglion cells increases with the depth of the narcosis. At any rate it ought to be always present in our mind that the deeper the narcosis the more it inhibits oxidation processes, and that the ganglion cells of the cerebral cortex are exceedingly sensitive to lack of oxygen. Here we deal with the most tender and perishable cells of our body.

In this connection I wish, before concluding, to point out an error that has been handed down from olden times, and even at present has not been corrected everywhere. It is the identification of narcosis with sleep.

The origin of this confusion is evident. It is based on the entirely superficial analogy that both states are characterized by loss of consciousness. But not every loss of consciousness is sleep. This confusion, which may have been justified in

earlier times, when both conditions were known only by their external symptoms, is to-day, when we have penetrated somewhat more deeply into the inner processes of the cells of the cerebral cortex, a grave mistake. Closer consideration will show this plainly.

What occurs in the neurons of the cerebral cortex during an act of consciousness? I am far from intending to give here a detailed analysis of these processes, I wish to emphasize only a single general fact. Let us conceive a condition of the cerebral cortex in which the neurons are in metabolic equilibrium; that is, in which the two phases of metabolism, the anabolic and catabolic phases, balance each other. We should have then a state of complete rest, in which no act of consciousness takes place. An act of consciousness ensues only when the metabolic equilibrium in a chain of associated neurons is disturbed by an exciting stimulus which causes a sudden increase of the catabolic phase. Every act of consciousness is the expression of a catabolic disturbance in the cortical neurons. This is not merely an assumption; it is shown, among other things, by the fact that even the simplest conscious process requires the associated co-operation of several ganglion-cell stations, and that on the other hand the nerve fibers which provide for this associated co-operation conduct no other impulses except catabolic excitation processes. On this general basis, for all processes of consciousness there are two possible origins of unconsciousness. Loss of consciousness will occur either because the ganglion cells are depressed, so that the external stimuli produce no excitation, or because exciting stimuli are absent. As we have seen, the first condition prevails in narcosis; the irritability is so much depressed that stimulation is ineffective. In sleep, the second alternative is predominant; the first plays at most the rôle of a predisposing part for the induction of sleep. We sleep, and determine the moment of going to sleep, by limiting as far as possible the sensory stimuli, especially the optical. This state of the utmost exclusion of external stimuli lasts throughout the entire period of sleep. This is supported to a certain extent by fatigue, that is, the decrease of irritability, which the ganglion cells have sustained by the constant action of sensory stimuli while awake during the day. A comparison of the processes which occur in the ganglion cells of the cerebral cortex during sleep and during narcosis will show us plainly how diametrically opposed these are.

During sleep, restitution occurs. The irritability, which becomes reduced in the course of the day as a result of the fatiguing action of sensory stimuli, gradually rises again. The fatigue of the ganglion cells, which, as we know, depends only on a relative lack of oxygen, becomes completely dispelled. The supply of oxygen, which during constant activity was not quite sufficient to keep irritability at its maximum, is, after the cessation of functional demands, fully sufficient to banish the fatigue. In short, during sleep, restoration occurs principally by the action of oxygen. In the morning the ganglion cells are refreshed and possess their full capacity for work.

How different is narcosis! In narcosis there is, on the contrary, as we have seen, a depression of the oxidation processes. The experiments showed that even with a free supply of oxygen a fatigued ganglion cell did not recover at all during narcosis. There occurs, rather, a gradual asphyxia, and, although this process is only developed to a small extent in light narcosis, still it presents just the reverse of that which sleep brings to the ganglion cells. In the one case, recovery from fatigue by oxidation; in the other, prevention of restitution by inhibition of the oxidation process. There can be no confusion between sleep and narcosis.

If we use narcotics to induce sleep, we must always bear in mind that no true sleep occurs as long as the narcosis of the cortex lasts. We can speak of "hypnotics," or "remedies for sleep" (*Schlafmittel*), only in the sense that, when there is constant excitation of the ganglion cells, they reduce irritability and induce a greater degree of depression, so that true sleep may take place as the narcosis passes off. In that sense a hypnotic may prove beneficial in the hands of the physician, and when used sparingly. The physician must, however, never forget that not the entire period of unconsciousness which follows the use of the hypnotic is true sleep, but that at first it is, rather, a depression, the injurious effects of which will manifest themselves when the hypnotic is used for a longer period.

Ladies and Gentlemen: I am at the end of my lecture. The facts which I have stated take us, I believe, a step forward in the analysis of narcosis. They show us the general nature of the process, which is merely one of the great group of depressive actions which depend on a disturbance of the oxygen metabolism. They open however, at the same time, a number of new questions. The previously mentioned hypothesis concerning the method by which narcotics inhibit the process of oxidation, shows us the direction in which these questions lie. It may serve us as a guide for the present. The further analysis of the process will principally have to determine the nature of the transmission of oxygen and in what way this is affected by the narcotic. The experiences of modern physical chemistry will be of great help to us in the study of this question. I may, however, take this opportunity of warning against a misuse of physical chemistry in the explanation of biological facts; and this the more, since this misuse, which has grown with the development of that science, is already beginning to arouse in the minds of many biologists a strong distrust of the value of physical chemistry in the analysis of biological processes. It is frequently believed that a biological process is explained when the terminology and certain catchwords, I might almost say the scientific "jargon," of physical chemistry have been applied to biological relations. There has been recently, for example, a great misuse of the word "colloidal process." There is positively nothing gained by it when a biological phenomenon (for instance, excitation or depression) is designated as colloidal process. This is neither correct nor incorrect; it says nothing. That the living tissues contain various colloid substances, and that these colloids undergo alterations in the course of the vital processes, has long been known. We wish, however, to know what it is that happens to the colloids, which of their properties are altered

and how these changes are incorporated into the machinery of the cell. For this purpose patient and careful analysis is required, and not the introduction of mere catch-words. The methods and results of physical chemistry give us very valuable material for such analysis; but it would be very one-sided to consider the methods of physical chemistry only. The methods and results of chemistry, physics and microscopical research must be employed, as well as those of physical chemistry. In short, every method must be employed which will bring us a step further. That alone can be the general principle of all physiological research, and this principle will also lead up to new knowledge in the investigation of narcosis.

A BRIEF NOTICE OF FELIX PLATTER, WITH EXTRACTS FROM HIS MS. MEMOIRS PRESERVED AT THE LIBRARY OF BÂLE.[1]

By Charles Greene Cumston, M. D., Boston, Mass.

In selecting the subject of Felix Platter for an address, I have done so because the man has been little known, although undoubtedly his reputation as a physician, as well as his writings, are certainly familiar to those of our profession who are more or less occupied or intimately concerned with the history of medicine.

Then again, I shall refer to his memoirs, the manuscript copy of which is preserved in the University of Bâle and I believe in giving extracts therefrom, which relate more particularly to medicine, a certain amount of interesting matter heretofore unknown to many medical historians, will be brought to light. Among the numerous manuscripts from the hand of Felix Platter deposited in the Public Library at Bâle, are to be found something over two hundred detached leaves which, so to speak, together form a diary, although they contain much information quite foreign to the person of the writer. From these MS. leaves I have selected only those portions pertaining more particularly to medicine and I must confess that they give the best description of student life and medical customs of those early days that I have ever come across. The time and place of study were those of the great philosopher and erudite Rabelais. What more need be said?

The subject of this address was born in 1536 of a distinguished father, Thomas Platter. Of his early life little will be said excepting that when Platter was very young he evinced a pronounced taste in the first place for poetry and music, then afterwards for show and dress which considerably occupied his thoughts. Nevertheless, the paternal advice always stood fast by him: the Dukes of Wurtemberg and the sister of Henry IV, Catherine, Duchess de Bar, were desirous of attaching him to their courts but in spite of their brilliant and reiterated offers he refused to leave Bâle. Besides Catherine de Bourbon and the Princes of the house of Wurtemburg, to whom he gave his professional care for more than forty years, Felix Platter comprised among his clients the Margraves of Baden and Brandebourg, the Dukes of Lorraine and Saxony. The most distinguished physicians of the time, as well as scientific bodies, had recourse to his knowledge. By a fortune always rare in a small country, his talents were promptly recognized and accepted by his compatriots. Received Doctor of Medicine at the age of twenty-one years, he was immediately elected member of the "consilium medicum." He had not, however, attained the required age and much comment was again made when the chair of the practice of medicine was confided to him in 1571, at the death of Jean Huber to whom he also succeeded by unanimous decision of the Council in the functions of city physician, or as it was termed *archiater,* which position invested with him the direction of the hospitals as well as the care of watching over the public health. He retained this position to the end of his life, in other words during a period of forty-three years. At the time of the plague of 1563-'64, his devotion obtained for him a universal gratitude. While several of his colleagues were careful of their person and another fled to Frankfort, Felix Platter supervised everything. The epidemic carried off his servant and a young man who was living with him, it seized upon his father, his mother, and all their household, but he fulfilled his duty with courage, braving the contagion at each step. Upon four other occasions, in 1576, 1582, 1593, and 1609, he was again face to face with the same scourge. Curiously enough, he and his wife were never affected; only upon one occasion, having committed the imprudence to hold the hand of a dying patient, a sore developed on his hand but fortunately the infection remained localized.

As a professor he was in no way inferior to the practitioner. A rich experience, a clear, methodical and penetrating mind, combined with an elegance of elocution readily explains why Platter became an eminent teacher and that his disciples loved him for his affable and gentle character, likewise his untiring zeal and enthusiasm. Haller (Biblioth. anat., 1, 255) calls him the star of the University of Bâle; this epithet is quite justified if one will reflect upon the impulse given to the Faculty of Medicine by Platter, seconded by Theodore Zwinger and Gaspard Bauhin.

Upon his return to his native town, Platter found only one or two medical students, but in the year 1575 there were already fifteen matriculated. From 1532 to 1560 only nine degrees of Doctor of Medicine had been given; during the twenty-five following years the number of degrees reached one hundred and fourteen while it attained four hundred and fifty-four in the period comprised between the year 1586 to

[1] Paper read at a meeting of the Book and Journal Club of the Medical and Chirurgical Faculty of Maryland, Baltimore, February 6, 1912.

1610. German, Dutch, Hungarian, Italian, French and English students flocked to Bâle and were proud of the honor of receiving their degree of M. D. from the University.

Two innovations contributed to this prosperity, namely, dissection and the creation of a chair of botany and anatomy. This initiative belongs to Platter. As a student at the Faculty of Montpellier, which at this time was distinguished from the majority of other schools in that each year the professors publicly dissected two or three cadavers, he had followed these operations with the greatest interest, overcoming the repugnance that his naturally timid and impressionable nature caused. He had hardly returned to Bâle when he performed an autopsy before a large audience, an event which had not taken place in that town since the days of Andreas Vesalius. However, the installation of Gaspard Bauhin as professor of anatomy and botany, the establishment of an amphitheatre and of a medicinal garden, only date from the year 1589.

Felix Platter only wrote late in life and he was nearly fifty when, in 1583, he gave the printer his work entitled: *De corporis humani structura et usu.* Then twenty years passed by before he published his *Praxeos medicæ,* the first volume of which appeared in 1602, the third and last in 1608. Many editions of this manual of pathology and therapeutics succeeded each other at short intervals up to the year of 1736, a success all the more remarkable because it corresponds to that period during which medicine was undergoing a complete transformation. And lastly, when nearly an octogenarian and having behind him fifty-seven years of practice, Platter published his *Observationum in hominis affectibus* which contained the fruit of his long experience.

If these works have not always been appreciated at their just value, it is usually because one has lost sight of the object for which they were written, viz., the instruction of students. Plater has particularly been reproached in that his first work, that on anatomy, contains only plates reproduced after those of Vesalius. On this point our author explains himself with perfect frankness, for he distinctly states: "As up to the present time the plates of Vesalius are the best that have ever been offered, and as it would be almost impossible to surpass them, I would have willingly added them to this volume introducing a few slight changes (because the opportunity presented itself for buying them), if I had not been prevented from this intention by the necessity of adopting under the circumstances a large size volume which would be very inconvenient for students. That is why I have had engraved on copper, reducing them in size and slightly changing them, the plates of Vesalius that I have completed by adding a few others." Several of the figures are new or present more details than those of Vesalius and, consequently, there can be no question of plagiarism on the part of Platter.

Scientific knowledge without literary culture produces a dryness of the mind and the development of pedantism, whose inseparable companion is a poverty of ideas. On the other hand much is due to letters in many a discovery made in various domains which are foreign to them. Thomas Platter impressed his son Felix with the importance of the dead languages and it was not likely, in point of fact, that these would be unknown to him at a time when, thanks to the vogue of Galen and Hippocrates, the chair of Greek was almost always filled by a physician. From this classical education, Felix Platter derived a promptitude of intelligence and a gift of analysis, two qualities which not a little contributed to his renown. In reality, his successes as a practitioner are in a less degree due to his complicated prescriptions, composed of thirty or forty ingredients, than to his great skill in diagnosis. His *Praxeos medicæ* is recommendable in the first place by a rational classification of diseases, which are studied according to their nature and not merely in relation to their seat. His observations on insanity give evidence of a remarkable insight to diseases of the mind and he protests against the heartless and barbarous treatment to which the insane were in those days subjected; he endeavored to obtain a cure by adopting a method which takes into consideration the moral phenomena, and, consequently, it is not too much to say that Platter was a fore-runner of the immortal Pinel.

In endeavoring to discover morbid causes by post-mortem examinations, Platter certainly inaugurated pathological anatomy. And, lastly, he pointed out the utility of exact statistics, when at the time of the epidemics of plague he drew up the census of the city, street by street, indicating for each house the number of its inhabitants, their names and their civil condition, the number of cases occurring in each epidemic, likewise the deaths, and all this work was undertaken when his mind was full of other medical preoccupations but which, nevertheless, remains as a most precious historic document.

This originality of view is quite in accord with the freshness of mind that the taste for poetry kept up in Felix Platter to the very last of his life. As an old man he was pleased to compose bits of verse both serious and light. When near his end he wrote his epitaph, a rough translation of which I will here give, although much of its beauty is naturally lost. "Upon this earth my vocation was to study the works of God and to apply myself, from my early youth, to turn them to His glory as well as to the well being of my fellow creatures. Now my soul enjoys celestial felicity: it contemplates the magnificences of the Lord, until that time when He shall resuscitate it with my body on the day of Judgment."

Plater was always a lover of music while plants and animals also occupied his leisure moments. His magnificent garden containing rare plants and vegetables which he himself cultivated, was the admiration of all. Rich was his collection of objects of art and natural history, which unfortunately was dispersed during the eighteenth century. The memoirs of de Thou, the historian, contain the following relative to Platter:

Il visita Félix Plater, docteur en médicine, logé dans une grande et agréable maison, et qui le reçut fort civilement. Plater lui fit voir dans son écurie une espèce d'âne sauvage, de la grandeur des mulets de Toscane ou d'Auvergne, le corps court et de longues jambes, la corne du pied fendue comme celle d'une biche, quoique plus grosse, le poil hérissé et d'une couleur jaunâtre et brune. Il lui montra encore un rat de montagne de la grandeur d'un chat, qu'ils appellent une marmotte: ce petit animal étoit enfermé dans

une cassette, et comme it avoit passé l'hiver sans manger, il étoit tout engourdi. Plater avoit aussi l'étui des fossiles de Conrad Gesner venue de Zurich, tel qu'il est décrit et dessiné dans un de ses livres. Cet étui renfermoit bien des raretés différentes, entre autres quantité d'insects particuliers, qui semblent autant de jeux de la nature. De Thou les examina à loisir et avec une grande curiosité, aidé de d'Amerbach, qui s'y connoissoit fort bien.

In the following year, viz., 1580, it was the turn of our dear Montaigne. In his "Voyage en Italie," speaking of Bâle the following paragraph will be found:

Nous y vîmes de singulier la maison d'un medicin nommé Félix Platerus, la plus peinte et enrichie de mignardises à la françoise qu'il est possible de voir; laquelle ledit médicin a bâtie fort grande, ample et somptueuse. Entre autre choses, il dresse un livre des simples qui est deja fort avancé; et au lieu que les autres font peindre les herbes selon leurs couleurs, lui a trouvé l'art de les coller toutes naturelles si proprement sur le papier, que les moindres feuilles et fibres y apparoissent comme elles sont, et il feuillette son livre, sans que rien en échappe; et montra des simples qui y étoient collés y avoit plus de vingt ans. Nous vîmes aussi et chez lui et en école publique des anatomies entières d'hommes morts, qui se tiennent. . . . Nous y vîmes [at Bâle] *force gens de savoir, comme Grineus, et celui qui a fait le Theatrum, et ledit médicin (Platerus), et Francois Hottoman. Ces deux derniers vinrent souper avec messieurs, lendemain qu'ils furent arrivés.*

Felix Platter died of dropsy on July 28, 1614, after a fortnight of great suffering. Only twice during his long life was he seriously ill. His wife had died eleven months before; their married life had been fifty-six years, and the only unhappiness casting a shadow over their union was the absence of children. They both left a large amount of money to be used for giving gratuitous medical treatment to the poor. Platter was buried in the cloister of the cathedral in Bâle and his stone, placed beside that of his father, bears the following inscription:

C. S.
Archiatro Basil. Dignissimo,
Urbis imo orbis Aescvlapio,
Acad. Professori Celeberrimo
Annos XLIII, Continvos,
Qui Rector Magnif. Sextum Fuit,
Quique Uno in Coniugio exoptatiss.
Cum Magdal. Ieckelman Matron. Lectiss.
Ante Annum Pie Defuncta,
Maritus vixit Annos LVI.
Doctor Vero Annos LVII.
Felici Platero Thomae F.
Naturae, Artisque Operum
Indagatori Solertissimo,
Conquisitori copiosissimo,
Medicorum suae Aetat. Principi
Nomine et Omine Felici,
Viro Probo, Probis Omnib. Probata,
In Egenos Liberali,
In Omnes Officioso,
Phthisi Sen. in Sed. Beat.
Sublato:
At Salutaribus Inventis,
Ingenilque Monumentis,
Aeternum Victuro,
Thomas Platerus D. Prof. Anat. Bot.
Fratri, Potius Patri Desideratiss.
M. H. P.
Vixit Annos. LXXVII M. IX.
Obitt Anno Sal. M. D. C. XIV. IVL. XXIIX.

I will now make extracts from Platter's diary, only selecting those portions which bear directly on his student life and medical subjects. I would point out that Catalan was an apothecary at Montpellier with whom he lived during three years that he studied in this city and that the Dr. Saporta to whom he refers was a famous professor and practitioner whose family originally came from Spain and whose ancestors were well known physicians in the epoch in which they lived. Rabelais refers to Saporta as a fellow student. Platter arrived in Montpellier some time in the latter part of October, 1553, and returned to Bâle on February 24, 1557. After giving a thrilling account of his journey to Montpellier and of his arrival in that city he says:

I at once began to follow the lectures. As is the custom each student chooses a preceptor, to whom he may refer for advice, and so I selected Dr. Saporta. I gave myself up seriously to the study of medicine; I listened to two or three lectures in the morning and as many in the afternoon. The letters and pressing exhortations of my father greatly stimulated me; I worked with great zeal, which greatly pleased my old host Catalan. He always spoke Latin to me according to his way, that is to say very badly, and when I replied in a rather more correct manner, he was very greatly astonished.

The running of my master's house was extremely economical, following the Spanish custom. It should be known that the Marans[2] do not use any of the food which the Jews abstain from. On the days we eat meat we had for dinner a mutton soup (but rarely beef) with small turnips and cabbage; it was good but the bouillon was not abundant. Each one had his plate and ate with the fingers. Afterwards came the roast. The wine was not wanting; it is a dark red and is mixed with much water. You have the servant pour for you into your glass the quantity of water you desire, then the wine is added; the servant throws away the wine that you leave because it cannot be kept for more than a year as it rapidly transforms into vinegar.

My master changed his pharmacy. I followed him to his new spacious and pleasing house. A room was given me for my use. Later on, with plates, I arranged the upper room for a study; I ornamented it with pictures, my host had a guilded arm chair put in for me (because he always took good care of me), so that when people came into the room each one was in ecstacy. The hall ended upon a beautiful terrace from which the entire city could be seen; the view extended as far as the sea, whose grumblings I could hear from time to time. It was here that I sat while studying; I cultivated the Indian fig tree which was developed from a slip sent to him from Spain. Often I sat at the window and played the lute; the people who lived opposite, a Monsieur Saint-George, and particularly his sister, Miss Martha, listened to me with pleasure.

With the advent of the new year a large number of diversions commenced, particularly gallant serenades at night in front of the houses. The same individual played upon the cymbals, drum and fife; the hautbois was also known, even quite generally played upon while the violincello and guitar were just becoming fashionable. The notable bourgeois gave balls to which the young ladies were taken; after supper dancing in the torch light was resorted to. These assemblies continued until daylight. The balls only ceased at the last day of the carnival.

We celebrated Epiphany at the Collegium among us Germans; the old beadle prepared the delicacies and the cake; Andreas de Croatie got the bean. Two days later we again celebrated

[2] The Marans were the descendants of the Moors that Ferdinand, the Catholic, expelled from Spain. Many came to Montpellier.

Epiphany at the house of Rondeletius.[3] As the Germans were reconducting by torch light some of their comrades, they were accosted by the captain of the watch who started to disarm them. From this resulted a great tumult in front of my host's pharmacy. Stephanus Contzenus obstinately refused to give up his dagger; Master Catalan having come out, begged him to give the arm to him; this was done and order was again restored. On the very next day the Germans made a complaint before the bailiff for violation of their franchises. The captain was blamed and we were assured that such an abuse would not occur again.

On the Sunday of the Quinquagesime (our *Herrenfastnacht* (Shrove-Sunday)), there was dancing throughout the entire city; everywhere accords of music could be heard and everywhere there were masquerades of a thousand different kinds. These festivities continued on Monday and the following day, which is called Mardi gras. On this day the young people form a procession: around the neck they carried a bag filled with oranges (their very low price in this country, a dozen only costing about two cents) and a basket on the arm in guise of a shield. When they reached the Place Nôtre-Dame, they began throwing the oranges at each other's heads and soon the pavement was covered with the débris. On the same Tuesday, the doctors of law went through the different quarters of the city disguised.

With Ash Wednesday Lent commences, during which it is forbidden, under the penalty of life, to eat either meat or eggs. It is quite true that we Germans transgressed this order by stealth. It was at this time that I learned how to spread butter on a sheet of paper, break the eggs on this and cook them over the heated coals; prudence demanded that no utensils should be employed. During Lent I cooked eggs over the candle, they being spread on buttered paper, and then I threw the shells into my study; later on a servant discovered this mass of shells; she told her mistress who displayed a very marked displeasure, but did not push the inquest any further. It is the custom to break the pots which have been used for cooking meat and to buy new ones in which to cook the fish.

A gentleman, one of our neighbors, invited me on a certain day to a nocturnal concert in honor of a young lady; this is what is called an aubade. At midnight we came before the house. We commenced by beating a drum in order to wake up the inhabitants of the quarter; then trumpets were heard, afterwards the hautbois, after the hautbois the fifes, after the fifes the violincellos and lastly three lutes, the entire performance lasted certainly three quarters of an hour. We were then conducted to a pastry cook where we were largely treated; we drank muscat and hyppocras and the night was passed in festivities.

My father sent me two beautiful skins dyed green; I had a garment made with them embroidered with green silk in which I strutted about and excited the envy of the gentlemen at the assemblies of dance. I arranged with a lame boot maker, whom we called Vulcan, that he was to bring me a new pair of shoes each Sunday; for the entire year this only cost me three francs, that is to say ten of our batzen.[4]

Although there are many physicians who do not take the trouble to become learned in their art, I always felt myself forced to learn everything that a doctor should know. At each instant I repeatedly heard how many physicians there were at Bâle; consequently, at my return there it would be necessary for me to make my way and even to rise above my colleagues. On the other hand, I was fully aware that my father was laden with debts, that his position only gave him a small compensation, that his boarders were his principal financial resource, and that, consequently, it would hardly be possible for him to help me. He himself wrote me to in no way count on his fortune, that he was not a rich man, but merely a schoolmaster, a poor peasant; that I was to make my calculation as if I had no fortune to be left me, or at the most a very small amount. How could one then foresee that he would again marry at a very advanced age and that he would bring forth such a numerous posterity?

All these circumstances caused me not only to study and follow the lectures with assiduity, but also to attentively watch in the pharmacy the manner in which medicines are prepared. My master had a large practice: consequently I derived much profit from the time spent in his laboratory. And still more, I collected a large number of plants that I delicately fixed on paper. But above all things I was desirous of knowing anatomy. I, consequently, never failed to be present when a cadaver was secretly opened. At the beginning, this operation was extremely repulsive to me; nevertheless, with some Welch students, I ran more than one risk in order to obtain subjects. Frequent dissections took place at the house of Gallotus, who had married a lady of Montpellier and enjoyed a certain fortune. He convened us to go armed outside of the city to dig up secretly, in the cemeteries adjacent to the cloisters, the bodies which had been buried on the same day; we carried them to his house, where we proceeded to the autopsy. Certain individuals were present at burials and then they would lead us to the grave.

My first expedition of this kind dates from December 11, 1554. The night was already dark when Gallotus lead us outside the city to the monastery of the Augustins. We there found an adventurous monk who had disguised himself and gave us his help. We entered furtively into the cloister, where we remained drinking until midnight. Then, well armed, and observing the greatest silence we went to the cemetery of the convent of St. Denis. Myconius had his sword drawn while the Welchmen had their daggers unsheathed. We dug up the corpse with only our hands, because the earth had not had time to become compact. When once the cadaver was brought to light a rope was passed round it and, pulling with all our might, we brought it up to the surface; after having enveloped it in our cloaks, we carried it on two rods up to the entrance of the city. It might have been about three o'clock in the morning. We placed our load in a corner and then knocked at the gate. An old porter presented himself in his shirt and opened; we begged him to give us a drink, pretexting that we were dying of thirst. While he went to get the wine three of us brought the cadaver in and carried it to Gallotus' house which was not far away. The porter suspected nothing. As to the monks of St. Denis, they found themselves obliged to guard the cemetery and from their cloister they fired with their arbalest[5] on the students who presented themselves.

The theatrum often served for dissections, which were then presided over by a professor; a barber manipulated the scalpel. Beside the students the audience contained a large number of noblemen and citizens, ladies as well, even when one dissected a male; many monks also came there. I exercised myself a little in distilling. I took note of a large number of receipts that the doctors gave me or which I borrowed from works of Falco; the latter were inherited by my host from Falco himself; he kept them under key in a room into which I introduced myself by a ladder not without danger. I was also indebted to the knowledge of excellent remedies either to Kirchmannus who had them from the physician Faber, of Cologne, or to students who brought them back from Italy and with whom I discussed science. I put in writing the *loci communes in tota medicina;* I reduced into tables the most important books of Galen; I heard Rondeletius express his strange opinions of which I took careful note. Once we passed

[3] Rondelet was a very celebrated physician and Chancellor of the University of Montpellier. The character of Dr. Rondebilis in Rabelais' writings is simply a caricature of the eminent professor.

[4] A batz was a piece of money used at Bâle, in value being about six cents

[5] A cross-bow.

an entire night copying a book: *De componendis medicamentis*, that Rondeletius loaned us; we were careful not to omit a receipt for causing hair to grow, because still being without a beard, we thought that a mustache would give us a more respectable appearance: how many times in the evening have we besmirched our lips, which resulted in soiling the pillows; we also scraped under the nose with a razor, but all these fine means were not at all efficacious.

At this time, Humelius informed me that his pharmacy was not at all profitable, that few remedies were prescribed, that the people of Bâle were not at all anxious in having skilful physicians, that the prescriptions were rather more German than Latin. The majority of physicians purged with senna, licorice and other absurd receipts. Dr. Isaac conducted himself as a quack of the lowest order. In brief, it was better to be a beggar than an apothecary at Bâle. All that the physicians knew how to do was to purge; as to potent medicines, like those prescribed at Montpellier, there was no question of them. Humulius, consequently counted on me to reform this condition of affairs. His letters stimulated me; I could foresee the possibility of rising above my colleagues and of introducing several novelties such as the enema, topics and a large number of excellent specifics. By the grace of God this did happen.

My father warned me not to permit myself to care for my German comrades, on account of the punishment that one ran the risk of receiving at Montpellier if one practiced the art of healing without having a diploma: such offenders are placed astride the back of an ass, facing the animal's rear, whose tail they hold in the place of reins; then they are led through the streets in the midst of the laughter of the populace, finally they are conducted out of the town and during the entire course the children amuse themselves by covering them with mud.

On March third, 1555, Guilelmus Eduardus was received doctor of medicine. The promotion, presided over by Saporta, was celebrated in the church with great solemnity and to the sound of organs. The recipient rendered grace in five or six languages, among which German, although he did not know the others. He was given a very pleasant promenade through the city; a silk plume decorated his square bonnet; the hautbois played; branches of cinnamon and little figures of sugar were carried in the processsion. There was a magnificent collation: more than a quintal of dragées were thrown about; the hyppocras was excellent; afterwards came the dancing.

On May 28th, 1556, I was received bachelor of medicine; Dr. Saporta performed the promotion at the *collegium regium*. The doctors of medicine of the University argued against me; the actus lasted from six to nine o'clock in the morning. After which I put on a red robe and rendered thanks by a carmen in which the Germans were not forgotten. In the beginning, I had recited by heart a long oration. Finally I paid eleven francs and three sous, for which I received a diploma bearing a seal. The Germans presented their congratulations to me; in order to show my appreciation, I offered them a banquet.

About this time a tumult occurred. The students reproached the professors for not giving their lectures. They assembled and armed they marched around the college and those who were there listening to a lecture were invited to come out and join the rest. It was thus that Hoechstetter came to ask me to join while I was at Saporta's lecture; I did not feel like giving offence to this professor, but Hoechstetter would not listen to me and I was finally obliged to go towards the house of parliament with an enormous crowd of students of all nationalities. There our procurator complained in our name of the neglect of the doctors and demanded the re-establishment of the ancient custom by which two procuratores, elected by the students, were invested in the right to retain the stipendia belonging to the professors who failed to give their lectures. The doctors replied by the mouth of a procurator; nevertheless, our request was granted and the tumult subsided. My father wrote me how happy he was to think that we Germans were not disturbed on account of religion. As it had come to his ears that I was quite as good a dancer as a lute player, he ended his letter by begging me not to become in love with a Welch girl, because he was doing everything in his power to give me a most agreeable wife as soon as I should return to my native country. He revealed to me the negotiations he had commenced with Master Franz Jeckelmann. The latter did not say no, but he wished to await my return before deciding anything. My father highly praised the young lady, her virtues, her judgment and her docility. He had for a long time suspected, and my comrade Hummel had recently confirmed him in this idea, that the young person was pleasing to me; for this reason he made me these overtures sooner than it was perhaps proper, but so that I would be all the more hasty in completing my *cursus studiorum* and return to Bâle. He advised me to follow my studies with ardor and not to neglect surgery.

"Great," said he, "is our penury in surgeons; the majority are children who are lacking in knowledge and experience. A difficult case comes up (?) They tremble like wet hens, scratching their heads in secret but before people *promittunt salutem*. What is the result? The patients remain deformed, when they do not die. It is necessary under such conditions that the physician should know how to advise and give assistance or even take the knife in hand; the profit is quite worth the trouble. My son, the desire of thy father is to give in thee to the country an honest man, distinguished and useful. At Bâle the number of physicians is frightful and if one is not capable of surpassing his confrères, one is sure of remaining for all his life a kind of beggar unless he should become an aulicus and engage himself in a foreign country. Now, above all things, I want to guard thee with us. He who has the greatest talent is the one who will espouse the wife of his choice."

I wrote home, admitting that the young lady had been dear to me for a long time; I only asked for the time to be received doctor and to return to my country, because the hope of obtaining her hand removed from my thoughts any idea of settling elsewhere than in Bâle. I added that the will of her father was not sufficient, that it was necessary to obtain her consent, and I begged my father to find out her sentiments when the occasion should present itself. One night I dreamed that I had a pain in my hand and that I went to consult the barber Jeckelmann, when his daughter applied something to the suffering member and I felt myself healed. Upon awaking I took this dream to mean a promise of our union.

Some time after this several of my compatriots and school friends arrived at Montpellier. They carried long Swiss swords, their costumes being completely German. One would have taken them for German foot soldiers, their manners were gross. By them I received a large number of letters. My father informed me how he had acquitted himself of my errand, viz. to ascertain what I desired to know: an enterprise not easy of undertaking, because the young lady only went out to go to church, without taking into consideration the fact that rumor was abroad that there was an understanding between herself and me. Finally my father was able to speak to her alone: he told her that I desired to know if she took pleasure in my person and if, God helping, she would accept me upon my return when I should ask for her hand. Blushing, she had replied that what pleased her father would also please her; she had always heard me spoken of favorably and had always held me in high esteem. For that matter, for a long time I had been most agreeable to her and this fact she had let be seen by the god-mother of her father, the old Schultheiss Fren, because she had admitted to the latter never to have felt for anyone as much inclination as she had for me. Consequently, she would wait for me. She had the intention of

going on a certain Sunday on a promenade with the family in the neighborhood of Gumdeldingen, and my father proposed to offer them a collation. It is readily comprehensible that this letter filled me with joy and courage. I sent Master Jeckelmann and to his daughter two beautiful embroidered cushions, some excellent Cyprus wine and two large branches of coral.

On August 25th, 1556, I received letters from Bâle, among which five sheets of paper folded like a book in octavo and completely covered with my father's writing. He showed that he was satisfied in knowing that I was working steadily to arrive *ad gradum;* he hoped that the next year would see me back in my country because Master Jeckelmann commenced to be impatient: numerous pretenders to his daughter's hand, several of whom of very excellent family, did not allow him any rest. My father also perceived that, on account of the good will which she had towards me, my future wife would salute my return with pleasure and that she sighed for that time to come. "And those who have been refused repeat: We want to see what a fine doctor he will make, he who supplants us in the estimation of Barber Franz! Have I need of telling you more along these lines? The entire city is filled with the news that Master Jeckelmann has assuredly promised thee his daughter and that from this time on it is useless for anyone to present himself. If thou couldst only hear all the talk which is made it would excite thee to confound some day those who reproached thee with thine happiness. But if thou preoccupy thyself above all to render glory to God, to fill me with satisfaction and be useful to the country, there is more than is necessary to encourage thee in thine work." My father also said that I would receive great praise by taking my degree of doctor at Bâle rather than elsewhere: the magistrates and the bourgeoisie would look upon this with a better eye than if I imitated those who take their promotion in a foreign country and who are reputed too incapable of taking the degree at our university; because one knows the saying: *Accipimus pecuniam et mittimus stultos in Germaniam.*

In November 1556 I resolved to return to the paternal roof in the following spring, by the way of Toulouse, Paris and France. My host bought me a horse and supplied me with the necessaries for the journey; my father had some money waiting for me at Paris. I was to have a companion, Theodorus Birckmannus, of Cologne, an erudite young man who not only knew how to play string instruments, but also the fife, so that is was easy for us to amuse ourselves upon the slightest occasion during our journey. A neighbor sold the horse and I disposed of my good lute not without regret. The twenty-fourth of February we treated our comrades at the inn and bade them good-bye. I called upon my professors and other acquaintances, also upon a few young ladies. The twenty-seventh of February I bade good-bye to Monsieur Catalanus who cried, likewise his wife and his servants. Brickmann arrived in front of the pharmacy with the Germans who wished to conduct us on our start. I straddled my horse and, God aiding, but with a very heavy heart in leaving this good city where I had so long time dwelt, I started off escorted by quite a numerous suite on horseback. Then I was seized by fright in thinking of the dangers which might assail me during the long trip and at the thought that I would never again see Montpellier, my heart became tender, my eyes moistened with tears.

As has already been pointed out, Platter arrived in Bâle early in the year 1557 and I will now quote his description of the taking of the degree of doctor of medicine in his native city, which is all the more curious and interesting, because it is a description given by the candidate himself.

The time had come to take my doctorate. Wishing to furnish a preliminary proof of my knowledge before making an official demand, I begged of the Faculty of Medicine the permission to profess at the *collegium* during the canicule, which was at once accorded me. Immediately I prepared myself. I sold my horse for one half of his original cost; my father took the sum, so that I was very short of money. Great was my ardor in working. On July 21, after having, on the preceding Sunday, put up notices on the doors of the church that I was to give a course of lectures, I gave my first lecture at the *collegium* in the *aula medicorum.* I commenced by a long peroration. Then I undertook the explanation of the *liber Galeni de causis morborum.* At the beginning nearly all of the doctors and the majority of the professors figured in the audience, but at the end there were only two Dutchmen remaining. On going out from the lecture they accompanied me to my home, climbed the mulberry trees in my father's garden and regaled themselves with their fruit. I showed them some curiosities in order to encourage them to follow my lectures with assiduity.

On August 14, I went to Dr. Oswaldus Berus,[6] Dean of the Faculty, and in an oration I postulated the *gradus medicus.* Thereupon I was assigned for the next day, Sunday afternoon, at the house of this same Dr. Oswaldus behind the cathedral where the three professors composing the *collegium medicum* met together. After having heard my harangue requesting the degree, they finally came to the censure: I proved that I had studied for so many years, then I showed my diplomas of Master and Bachelor of Medicine obtained at Montpellier. The professors appeared satisfied; but when they asked my age and I replied that I would be twenty-one years October next, the Decanus entered into a discourse in order to declare that the candidate should be at least twenty-four years of age. They consequently sent me away. I entered my home extremely put out, persuaded that my youth was to be an obstacle to my promotion. The same evening I told my troubles to my future father-in-law; he became angry: "If they make any difficulties," cried he, "I will give you my horse and you may go and obtain your diploma at Montpellier." However, I tormented myself gratuitously because the professors had not taken seriously their objection and they regretted that I had left so quickly.

On the next day, August 16, the beadle came to notify me for the *tentamen,* which took place in the house of Dr. Oswaldus before the three same personages. They interrogated me lengthily, particularly on medical questions; I replied to them with alacrity, it was not as difficult as I had imagined. The examination lasted three complete hours, after which they gave me the two *puncta* to explain the next day, viz., an aphorism of Hippocrates: *mutationes temporum pariunt morbos,* and the *definitio medicinæ Gal. in arte parva: medicina est scientia salubrium,* etc. At the end of this séance, Margaret, Dr. Oswald's daughter, served us with cake and wine; then the professors were extremely gay with me; for that matter, it was I who paid.

I passed the examination the next day, August 17, in the same place. I was compelled to expatiate *memoriter,* for the lapse of about an hour, on the *themata* which had been given me, just exactly as if I were professing. Then the three doctors took up the speech in order to refute my argument and this lasted full three hours; Dr. Oswald especially, who considered himself a great philosopher, worried me quite lengthily. Finally, I was allowed to retire; then I was called back and was informed according to custom, that in a short time I should be obliged to uphold a public debate. Following this we partook of a collation for which I paid, along with a little gift to Dr. Oswald's daughter.

I prepared myself for the debate. I received two short *themata*

[6] Oswald Ber, received doctor of medicine at Bâle in 1512, appointed professor in 1513, remained dean at the Faculty of Medicine from 1520 to the time of his death in 1567. He was rector in 1529 when the University was closed and it was he himself who re-opened it as rector in 1532.

from the Dean; they were not too much to my liking, and if the candidate had had, as he has today, the right of choosing, I should have preferred a more ample subject. I had these *themata* printed with a few commentaries, and on Sunday, August 29, they were posted at the four parish churches; the beadle carried copies to all the doctors and professors at the same time notifying them of the debate. This was fixed for the following Thursday. Now, on Monday, I was taken with fever, accompanied by a catarrh: it was a disease called the croup which was prevalent at that time. I was, consequently, very uncomfortable. The epidemic spread far and near. Later on I learned that it had appeared at Montpellier, at which place it was called the whooping cough. Nevertheless, on Thursday, September 2, I presented myself for upholding the debate which took place in the *aula medicorum;* it commenced at seven o'clock in the morning and lasted untill noon. Nearly all the academicians were present because there had not been a debate for a long time. The doctors of medicine alone spoke (there were hardly more than one or two students at this time; the professors Huberus and Isaacus gave them the lectures), but the masters of philosophy also mixed in with the discussion. By the aid of God, I got out of it not without honor. The seance once ended, I was obliged to regale an entire table full of guests at The Crown. After the repast, I hied myself to the usual meeting place to tell my joy to Madeleine.

On September 6, the members of the Faculty requested me to come to them in order to announce that I was admitted to the doctorate and to congratulate me. As soon as they had notified me at my house of the day and time of the promotion, I made the necessary arrangements. I had been assigned two promotores: Dr. Isaac, gave me the *themata* of my discourse, and Dr. Oswald Ber was appointed to give me the insignia. I had the notification printed, and the following Saturday, accompanied by Dr. Isaac and the beadle, I went to invite *ad actum* the burgomasters, scholars, academicians and a large number of my good friends, among whom my future father-in-law.

On Monday, September 26, I was conducted to the house of Dean Ber. Here we drank malmsey, then the procession proceeded to the *collegium*. I wore a garment of black woolen, embroidered on all the seams with a band of velvet the breadth of a hand; I wore red tights and a pourpoint of silk of the same color. In front of Dr. Huber's house, Dr. Oswald suddenly remembered that I should also dissert without preparation on a subject given at the time, and as he had forgotten to bring a book with him, he had one taken from the study of Dr. Huber.[7] We arrived at the *aula medicorum*. It was draped with rich tapestries and filled with people because for a long time back there had been no doctor's promotion. I took my place in the lower cathedra, Dr. Isaac in the upper one. The trumpets sounded, and Dr. Isaac having pronounced a discourse, proposed the *themata* to me. Immediately I recited my oration by heart, although it was long; then Dr. Isaac passed me over to the Dean and left the chair. Dr. Oswald received me with a short allocution, and preceded by the beadle carrying the sceptre, we mounted into the upper chair. There, with the customary solemnity, the Dean placed a velvet cap on my head and then upon it a beautiful crown; in short, he accomplished all the customary ceremonies, without forgetting the ring which he placed on my finger. After having proclaimed me doctor, he ordered me to give a sample of my knowledge by at once treating the first subject offered. He looked through his book and designated a place; I read as if the text of my thesis was found printed there, and then I began to dissert. After a moment, the Dean closed the book, saying that that was sufficient; then he gave me the privilege of speaking so that I might offer up my thanks, which I did in a long harangue that I had learned by heart. This was the last act of the ceremony; it had lasted more than four hours. The four trumpets again sounded and we left in procession to go to The Crown, where the banquet was prepared. The rector, Wolfgang Wissenburg, walked by my side; then came the venerable Dr. Amberbach and other academicians in quite a large number: in front of me the beadle and the four musicians marched, playing all the way. At the repast, there were seven tables; we were very well treated and it only cost me four batzen a head. The dinner ended at three o'clock because the banquets were not so prolonged then as they are at present. According to custom, the guests preceded by the sceptre were bade farewell to by Dr. Isaac. He then led me to his residence where we had a collation. After which I was conducted to the paternal roof.

Immediately after his promotion to the grade of doctor, Platter was married, the details of which happy occasion he enters into at length in his journal. What he says gives a very excellent insight into the customs of those days, but as I wish to hold to the medical portions of his journal more particularly, I shall immediately proceed to translate what he says of physicians and the practice of medicine at Bâle at the time he commenced.

At Bâle, at the time of my return, great was the number of those who practised medicine. Here is the list of the graduates: Dr. Oswald Ber, Physician to the City; Dr. Jean Huber; Dr. Isaac Keller; Dr. Adam de Bodenstein, called Carlstadt; Dr. Henri Pantaléon;[8] Dr. Gaspard Petri, called Mellinger; Dr. Guilelmus Gratarolus de Bergame; Dr. Jacob Huggelin; Dr. Jacob Wecker, the licentiate Philippus Bechius, and Joh. Bauhinus. I do not count Jacobus Myconius nor Dr. Jacobus Zonion who left after a short time. As to quacks there were: Ziliochs, of Saint-Alban, to whom one went to consult just like a physician, and the widow of Othon Brunfels who enjoyed a great reputation. To all these I added my own self and one year after, Dr. Theodorus Zwingerus[9]

[7] John Huber, of Bâle (1507-1571), a student of J. Sapidus, of Schlettstadt, studied more particularly at Montpellier and Toulouse. He practised medicine with success, was appointed professor of physics in 1544, a little later professor of theoretical medicine and in 1567, at the death of Oswald Ber, professor of practical medicine.

[8] Henri Pantaléon, born at Bâle in 1502, had frequently changed his profession and place of abode before being appointed, in 1544, professor of the Latin tongue at the Pædagogium, which did not prevent him from pursuing his studies in theology and medicine. Deacon of St. Peter, he obtained the licentiate in theology, but the ecclesiastical career did not appear suited to his character which was an enemy of constraint. After a time he gave up his functions as deacon and went to study medicine at Valencia, Avignon and Montpellier.

In 1558 the *concilium medicum* of Bâle received him in its midst. Pantaléon died March 3, 1595. Among his many writings may be mentioned his *diarium historicum* and the *Heldenbuch deutscher Nation*. Emperor Maxillian II made him Poet Laureate and also a palatin count.

[9] Theodore Zwinger, or Speiser (1533-1588), was a student of Thomas Platter and by his mother a nephew of the erudite printer Jean Oporin. He successfully occupied the chairs of Greek, Ethics and Theoretical Medicine at Bâle. It is said that his house had as tapestry only inscriptions in Hebrew, Greek, and German. Zwinger translated, at the same time adding commentaries, several works of Hippocrates and Galen, and composed among others, *Theatrum humanæ vitæ*, *Methodus apodemica* and *Physiologia medica*. His biography has been written by Felix Platter in the commencement of the *Theatrum*, in the 1604 Bâle edition. The account here given by Felix Platter is an honor to both these physicians.

swelled the list. Thus in 1557-1558, Bâle possessed nearly seventeen physicians. It was, consequently, necessary for me to strive if I were to make my livelihood; in this respect God has covered me with benedictions. At this time a certain Ammann was greatly extolled: he was a peasant at Utzensdorf to whom an extraordinary crowd rushed; the urine indicated to him the nature of the disease; during many years he performed curious practises which resulted in his making a very large fortune. After this individual the Jew Alsswiler was for a long time greatly sought after. In the *ruelle des Tanneurs* an old woman called Lülbürenen, also gave many consultations, likewise two executioners, Wolf Kaese and George Kaese; their elder brother had acquired a great renown as a physician at Schaffhausen, like his father Wolf, the executioner of Tubingen.

Patients from the middle class and nobility commenced to come to me. They submitted my knowledge to a singular test: they sent me their urine and I was to guess the disease. I did so well that several were greatly surprised at my replies and finally took the habit of consulting me. My clientele increased daily, not only in the city but also without. People came to Bâle for a stay to be under my care; others came and left at once, taking my prescriptions with them; or on the other hand, foreigners requested me to come to their houses and the castles; I went there with rapidity, hardly staying with them and regained my house as quickly as I had left. In this way it was possible to treat a large number of patients both near and afar.

In April 1559, a robber was to be tried: among other misdemeanors, he had broken into The White Dove, and taken away a wash tub. I begged my father-in-law, since he was member of the council, to have the cadaver placed at my disposal. Master Franz looked as if he thought my request would be rejected, because the University would claim the body; perhaps, also, he imagined that I would not know how to undertake a dissection. I was careful not to importune him further and I went to present my request to the burgomaster Franz Oberrieth. Although astonished in the first place that I should be desirous of undertaking such a labor alone, he evinced his good will toward me and promised to submit my request before the council the next day. On April 5, the criminal appeared before the court and was condemned to be decapitated. At the breaking up of the Council, my father-in-law came to tell me that the cadaver would be given over to me, which should be brought after the execution into the Church of St. Elizabeth, where I would have a permit to dissect it; only I was obliged to notify the doctors and barbers, so that they might witness the operation if they so desired.

Thus it was done. People of all conditions formed a numerous audience and I derived great honor from it because only a very long time before, not since Vesalius, had any public dissection taken place at Bâle. This work took me three days. I then boiled the limbs after they had been deprived of the flesh, I put them together, and had thus a skeleton that I still possess after fifty-three years. The mother of the robber was an over-seer of the women at the church of the hospital: many years had passed when one day she came to consult me. She had learned that the skeleton of her son was in my house; and in reality I had had a very nice show-case made for it in my room. This woman sat down on a bench quite near it, looked gravely at the skeleton without uttering a word; but when she went out she said to the people:

"Alas, will not one accord him a burying place?"

We now come to that portion of Platter's diary in which he describes the seven mortalities of Bâle, in other words, the seven visitations of the plague in this city. Although succinct, the description is most excellent and the statistics of deaths and recoveries are of very great importance, inasmuch as the figures demonstrate to what extent these ravages of former times went.

I remember that the first invasion of the plague occurred in 1539, 1540, and 1541, sometimes decreasing, at others redoubling its intensity. It lasted for three years, up to the end of 1541.

The second visitation of the plague took place during the years 1550, 1551, 1552, and 1553. It began towards the end of 1550, was extremely violent and killed many people. The following winter and even the spring time of 1552 were not so bad; nevertheless the scourge had not completely disappeared and in the autumn there was a very marked recrudescence in Great and in Little Bâle, which continued into April 1553.

The third plague, 1563 to 1564, was called The Great Mortality. It was extremely murderous although it did not last so long as the others. I had the opportunity of making myself useful to many people. The epidemic appeared in the winter of 1563; it extended up the Rhine and advanced to the Swiss countries; it disappeared towards the end of 1564, but it had time enough to carry away an extraordinary number of both young and old. Children were particularly afflicted, then the servants and workmen. Nearly all of those who, at the Saint-Jean, came back from foreign service, succumbed. The hospitals and the refuges were filled with the sick; among the middle class there were many victims, merchants and artisans, counsellors, savants, students, scholars and preachers. Pregnant women and those who had been delivered died for the most part. Likewise elderly people. At times, and I witnessed it, as many as twenty bodies were buried at once in the same ditch. The dead were transported without interruption from St. Elizabeth's hospital and were thrown into a large ditch; the latter remained open for several days until it had been well filled, and the bodies were only covered over by a very thin layer of earth. The streets were completely deserted; in the assemblies, at the churches and elsewhere, considerable emptiness prevailed and a number of widows and widowed were to be noticed. However, cases of cure after a long illness were far from being infrequent.

Although large, the number of victims is uncertain, because the deaths were not registered as was the case some years later. Thousands and thousands of deaths were commonly stated; this is an evident exaggeration. Dr. Sultzerus, at that time the first pastor, and myself who had to care for a large number of patients and who took notes of the deaths, we have, by calculating each on his own account, estimated the number of deaths at very nearly four thousand; for Bâle this can hardly be counted as small. At the hospital, according to the expenses of burial inscribed on the register from Februray 28, 1564 to March 24, 1565, I calculated that during this period the number of deaths must have been exactly two hundred.

As soon as the contagion was on its decline, and even while it was in its full blast, carrying away entire families, marriages continued to be contracted in full force. People remarried a few weeks after having been widowed; pregnant women, even nearly at their term, contracted second marriages, and the authorities were obliged to prevent them from taking a husband until a certain number of months had elapsed; widows and young girls were also ordered not to marry a stranger who was not a bourgeois, under the penalty of being expelled from the city.

The fourth mortality took place in 1576, 1577, and 1578. It broke out at Augst in the rue Blanche in 1576 at the house of a messenger who had brought it back with him from some unknown spot and who with his wife was the first victim, without counting that eight days later his brother-in-law and brother were in their turn seized upon. The plague spread from house to house and street to street, and soon it had invaded Augst and Bâle. It continued during the entire year of 1577, developing with more or less severity, sometimes here, sometimes there, up to the

THE ARMS OF PLATTER.
After a painting on glass at the Bâle Museum.

FELIX PLATTER, ANNO ÆTATIS 48.
After a portrait painted in 1584 by Hans Bock of Bâle.

spring of 1578; then it ceased. During these two years the number of victims was quite large.

The fifth mortality occurred in 1582 to 1583. It commenced towards the month of July 1582 and lasted into March 1583. During this short lapse of time it carried away many people, about one thousand and ninety-five individuals. The records of the hospitals showed me that from July 1582 to March 1583 one hundred and three people died, the larger number from the plague; it also shows that the total number of recoveries was one hundred and fifteen. At St. Peter, eleven people were buried in July, twenty-five in August, twenty-eight in September, thirty-nine in October, thirty in November, thirty-one in December, and twenty-two in January and February, 1583.

The sixth mortality appeared in 1593 and continued until the end of 1594. How many people were afflicted in this epidemic? This is a point upon which nothing absolute can be said, although it was in this very year that a record of births and deaths was commenced, these records being read on New Years' Day after the sermon of the evening. Five hundred and twenty-four people died in 1593 and nine hundred and two in 1594. If from these figures one deducts the average mortality in normal years, viz., two hundred and fifty, it may be supposed that in 1593 the epidemic carried away two hundred and seventy-four persons, and six hundred and sixty in 1594; total: nine hundred and twenty-six persons, both young and old.

The seventh mortality (1609, 1610, 1611) commenced in October, 1609. The plague was already present in the country of the Margrave, particularly at Loerrach, likewise in several places in Alsace; It appears that the apprentice of the baker Algenburg contracted it at Schopfen, where everyone was dying, and brought it back to the house of his master who lived in Little Bâle. In the first place, neither the ordinary symptoms of the scourge nor the head-ache made themselves felt, so that little attention was paid to it, although in Great and Little Bâle the number of patients and deaths was from time to time greater than usual. There was even doubt that it was the plague, in spite of the characteristic symptoms which appeared here and there; but in July the epidemic declared itself frankly and with an increasing violence. From October 12, 1610, from two hundred and fifty to two hundred and eighty-eight people were buried each week; finally in December the scourge decreased to about one-half and even more.

There were:	No. of cases	Deaths	Cures
In the five faubourgs	1720	1146	574
In the rest of the city....	2990	1913	1077
In Little Bâle	1039	724	315
At the hospital.....	659	185	474
Total	6408	3968	2440

In completing this recapitulation by means of the records of Saint Theodore and of the hospital, I find the total number of deaths comes to four thousand and forty-nine; there were one hundred and sixty-five families in which both the husband and the wife died.

TUBERCULOSIS IN INFANCY AND CHILDHOOD.*

By Henry Koplik, M. D., New York.

Tuberculosis is a disease not only prevalent and widely so in infancy and childhood, but is peculiar to this age. At this time its prevalence is widespread and it presents features so diverse from the same disease, as it occurs in adult life, that its study is of deep and startling interest. It is quite in accord with the pleasant changes of time and place that this subject should be considered before a society which bears the name of one of the great bedside observers of modern times. Lænnec was among the first to call attention to the unity of some of the forms of this disease in infancy and childhood with tuberculosis. Scrofulosis that syndrome peculiar to children was recognized by him to be nothing more or less than a form of tuberculosis.

I find it then appropriate that any analysis of this disease should take into consideration his great influence and should be the subject of an address before this distinguished body. The study of tuberculosis in infancy or childhood reveals its universal prevalence at this time of life, and lends support to the feeling that tuberculosis or its forms which affect adults or adolescents must, in a vast majority of instances, date from childhood. Moreover, a study of the disease in early life teaches forcibly the vast strides made in modern medicine through the study of pathology and experimental medicine. No disease illustrates this more completely than tuberculosis and no disease can show more enlightenment than tuberculosis in infancy and childhood through animal experiment. We can almost duplicate most of the forms of tuberculosis in infancy and childhood in the experimental laboratory. Through the work thus done and the light shed upon certain phases of the disease by experimental work we, to-day, feel more willing to explain hitherto obscure features of the disease and the reaction of the body cell against its essential cause, the tubercle bacillus. The clinical recognition of the various forms of tuberculosis in infancy and childhood has crystallized with greater certainty than even a decade ago at the bedside. Tuberculosis takes on phases and forms in infancy and childhood, and the infant organism reacts to the tubercle bacillus in quite a different manner from that of the adult. We will show that this is due to the soil in which the disease finds itself as distinguished from the adult and that the adult forms are distinctly peculiar and different clinically from the forms of childhood for distinct and experimentally proven reasons. No age is exempt from tuberculosis, and it is needless to assume any proposition tending to prove the contrary.

Much has been said and discussed concerning a so-called "disposition" to tuberculosis (von Behring, Ehrlich, Hamburger, Cornet). It cannot be said that infants or children are predisposed to tuberculosis any more than they are to measles or diphtheria, but one can say that, given an exposure to infection or the elements of infection they will contract tuberculosis, and also that they are in a position more than any one else to be exposed. They crawl along the floors, they are among

* Paper read at a meeting of The Lænnec, a society for the study of tuberculosis, The Johns Hopkins Hospital, January 29, 1912.

the poor crowded in with the tuberculous and phthisical; they put all things in their mouths, and their food—not milk alone—but other foods, such as candy, are more likely to come in contact on account of the habits of the poor with tuberculous material. Every child, therefore, infected with tubercle bacilli becomes tuberculous, and it may be said the disposition to contract infant tuberculosis is ever present in every child. Of course, the course of the infection will vary with the amount of infectious material introduced into the body and the individual disposition of the subject. Thus it will be shown that in certain individuals, as in very young infants and children, the tuberculous infection will run an acute course, in others a peculiarly protracted course (scrofulosis), and in older children the course of the disease will approach the forms seen in the adult.

We know that tuberculosis can be congenital not hereditary (von Behring), and we know that the infective agent may pass from the blood of the mother through the placenta into the body and organs of the fœtus. That tubercle bacilli have been found in the maternal placenta (Schmorl and Geipel), is well established beyond a question of a doubt, and that the bacilli can be found in the various organs of the fœtus with or without the formation of the tubercle is also proven (Rietschel, Sitzenfrei). That the fœtus can be born tuberculous and harbor tubercle bacilli and not manifest any of the signs or symptoms of tuberculosis is now an accepted fact (Baumgarten). It is true that in very early infancy, the first three months, there is an evident hiatus in the occurrence of tuberculosis, but we understand that this is so not because these infants are not tuberculous, but because at this period the tuberculosis may be inactive or latent. It is not necessary to assume that the sperma cell can carry tubercle bacilli or tuberculous poison to the ovum; this is a negligible factor in the face of all the possibilities which are mentioned from the maternal side.[1] Up to the second year of life, the incidence of active tuberculosis is less than at any other period. It increases from this time on and some authorities think that the time of greatest incidence of infections takes place at the fourth to the sixth year of life (Hamburger). The percentage of tuberculous children increases steadily up to the fourteenth year of life.[2] The course then takes a downward trend to adult life. Thus not only do the acute forms of tuberculosis diminish in later childhood, but the more chronic forms appear at this time proving that not only is tuberculosis chronic and curable in the sense that it annihilates itself, but that some of the forms are carried from later childhood and adolescence into adult life, where, on account of certain well established facts, tuberculosis takes on different forms from that found in children.

[1] Jani found tubercle bacilli in the genital organs of men suffering with tuberculosis. That bacilli can be carried into the uterus and adnexa has been demonstrated by animal experiment (Gaertner and Sitzenfrei). Tubercle has been found in the placenta of tuberculous women not necessarily in the advanced stage of the disease (Sitzenfrei, Schmorl).

Tubercle bacilli or tubercles have been found in the placenta, cord, decidua, fœtus and liquor amnii (Schmorl).

Congenital tuberculosis may occur in infants who have lived six months after birth (Rietschel, Sitzenfrei), and the infection can occur at any period, more probably toward the end of pregnancy in most cases. Cases of congenital tuberculosis have been published by Birsch Hirschfeld, Aschoff, Rindfleisch, Lehman, Schmorl, Kockel, Thierclin, Andrews, Hamburger, Sitzenfrei, Rietschel and Wollstein.

The infection from the mother through the ovum may be rejected, it takes place through the blood and placenta. This applies not only to tuberculous changes in the fœtus but in infants who die within the first half year of life.

Cases of congenital tuberculosis are certainly unusual and those in the first three months of life rare. I call attention to my early cases of tuberculous meningitis and the case of tuberculous peritonitis in an infant 4½ months old in whom tubercle bacilli were found in the fluid of the peritoneal cavity in large numbers.

Frequency.

The frequency of tuberculosis in infancy and childhood has been approached by various observers in various ways. It is quite evident that the results of autopsy are the most certain evidence, for here we can establish not only the healed or inactive or even the truly latent cases, but also the cases of active lethal tuberculosis. But autopsy material gives only a relative view of its frequency in the various strata of the population. Autopsy shows only those cases which have been in hospitals. Again one can approach the subject from the side of the district or family physician. This also has many possibilities of error for some physicians may not diagnose a case or conceal a diagnosis even should a census be taken of all individuals in any district. The modern methods of tuberculin diagnosis have enabled us to form an idea of the great prevalence of tuberculosis, but here again the material is drawn not from the population at large but from the dispensaries and hospital clinics. With these points well before us let us see the results of autopsy statistics as they are given to us to-day.

Taking large numbers of autopsies it is evident that the percentage of incidence will vary according to the number of autopsies. Thus in 16,581 autopsies Froebelius found that the first year of life showed an incidence of 2.5% of tuberculosis, the 123 autopsies of Harbitz 20.3%, Albrecht recorded 1300 autopsies with an incidence of 14.5%, Hamburger, 276 autopsies in the first year of life with an incidence of 4.5%, but none before the sixth month. Most interesting are the statistics of Hamburger taken from the autopsies made by Ghon at Escherich's clinic in Vienna. Taking 617 autopsies, tuberculosis was an accidental find in 17% of the cases in which the ages ranged from early infancy to the fourteenth year. These children died of all causes, and it is interesting that in them the accidental find of tuberculous lesions increased from 17% in the second year to 53% of all the cases in the 11th to 14th years, thus bearing out the assertion previously made that in adolescence the number of cases which carry their tuberculosis into adult life increases, especially from the seventh year.

[2] Naegeli, Hamburger.

Taking all autopsies of Ghon, 848 cases, the following table is instructive:

0- 3 mos.	105 cases of which	4%	were tuberculous.
4- 6 mos.	73 cases of which	18%	were tuberculous.
7-12 mos.	140 cases of which	23%	were tuberculous.
2 years	179 cases of which	40%	were tuberculous.
3- 4 yrs.	175 cases of which	60%	were tuberculous.
5- 6 yrs.	67 cases of which	56%	were tuberculous.
7-10 yrs.	65 cases of which	63%	were tuberculous.
11-14 yrs.	44 cases of which	70%	were tuberculous.

It is doubtful whether other great cities will show such a very marked preponderance of tuberculosis, and in fact there is reason to believe that they do not. In America the incidence will not be so great, for I do not believe from my studies that our poor are so badly nourished or so severely crowded as in Vienna. For the present it seems that other large cities of Europe as Zurich (Naegeli) show a very high percentage of tuberculosis as compared to Vienna. In the Charité at Berlin and the Berlin Orphan Asylum, Finkelstein calculates that of 5600 children of one year of age 72 are tuberculous.

Another way of gaining an insight into the frequency of tuberculosis in infancy and childhood is by means of the tuberculin skin reaction of von Pirquet and the *Stich* reaction of Epstein, Escherich and Hamburger. Epstein was, I believe, the first to call attention to the fact of the lack of reaction in the new born to tuberculin, and at the same time noticed the very important phenomenon of the *Stich* reaction, but it remained to von Pirquet to simplify the tuberculin reaction so as to nullify its ill effects and for Hamburger to point out that in those cases in which the cutaneous skin reaction of von Pirquet failed the *Stich* reaction might succeed and therefore was the most positive and delicate of all reactions, but more of this later.

von Pirquet took 988 children frequenting the Escherich clinic and found the following incidence of reaction to tuberculin:

0- 3 mos.	0%	2- 4 yrs.	37%
3- 6 mos.	5%	4- 6 yrs.	53%
6-12 mos.	16%	6-10 yrs.	57%
1- 2 yrs.	24%	10-14 yrs.	68%

Of 693 cases of inactive tuberculosis, that is children not suffering from symptoms of tuberculosis, he found 55% at the age of 10 to 14 years.

0- 3 mos.	0%	2- 4 yrs.	13%
3- 6 mos.	0%	4- 6 yrs.	17%
6-12 mos.	3%	6-10 yrs.	35%
1- 2 yrs.	2%	10-14 yrs.	55%

Thus one-half or more of the children (55%) of the poor who frequented the clinics for all causes other than tuberculosis, were tuberculous, that is, had tuberculous foci. Hamburger's statistics are still higher because he took the negative cases of von Pirquet and injected them with tuberculin and found that many of the children who did not respond to the cutaneous test did so to the *Stich* reaction. He found that between the 12th and 13th year fully 95% of the children of Vienna, among the poor, were infected with tuberculosis. Ganghofner of Prague obtained as high as 70% of infections. Hamburger states that the children of the poor are so situated that at puberty possibly all are infected with tuberculosis. If this statement may appear startling and in future found not to be quite apt, still it illustrates the main keynote of my theme, the startling prevalence of tuberculosis among the children of the poor in the large cities of the world.

The avenues or modes by which the tubercle bacillus may gain access to the body has been a subject of bitter controversy. It is not as yet absolutely established that this phase of the tuberculosis question may not receive additional light from future work. Until a recent date it has been accepted that aspiration or the aerogenous way was by far the most frequent avenue through which the infective agent entered the body (Weigert). Strength was lent to this theory by the fact that in a vast majority of cases, at least in children, the lungs were found involved. In recent times through the writings of von Behring and Schlossman light has been thrown upon the modes of infection through the digestive tract or deglutition.[3] In the heat of discussion this has been misinterpreted in some quarters to mean that von Behring especially emphasized the rôle played by cow's milk in causing tuberculosis in children. This is not exactly so. Schlossman has taken pains to point out that in supporting the theory of infection through the digestive tract, he includes all infectious matter entering the mouth, pharynx, œsophagus, stomach and intestines. This would include not only infected food but sputa in a moist or dried state adherent to objects, or anything which would introduce such infection, such as kissing, playing with toys infected with sputum, and foods. Schlossman contends, and this has been proven and accepted, that bacilli in the very young may thus enter the stomach and intestines, and, especially in infants, pass through the very permeable mucous membrane into the lymph circulation, leaving no trace, and from thence to the vena cava to be finally deposited in the end capillaries of the lung. It will be seen that this is an entirely different matter from the contention that through milk alone tuberculosis is in any appreciable percentage of cases a cause of infantile tuberculosis. All are agreed that the human subject is the main source from which emanates all tuberculous infection. In Vienna, Escherich and his school were at pains to prove that in a great percentage of cases infection could be traced to a person infected with tuberculosis who had been in the immediate vicinity of the infected child. It seems from a close study of my own experience in New York that I can give my unreserved support to this contention. I have been able to trace over and over again tuberculosis in parents as well as children and I have had several children under my care with symptoms of glandular, pulmonary and brain tuberculosis whose parents were either actively or inactively tuberculous.

It may be laid down as a fact that infection through tuber-

[3] Bartel and Spieles come to the conclusion as a result of animal experiment that infection by deglutition (dirt and smut) is the most frequent mode of contraction of tuberculosis in children.

culous milk, that is, not milk containing human tuberculous matter, but milk from tuberculous cows is rare. Such tuberculosis cannot form over one to two per cent of all the cases of tuberculosis that we know of, if indeed it reach that percentage. Since it has been possible to identify bovine and human tubercle bacilli, only 41 cases could be collected of tuberculosis in children caused by the bovine bacillus (Hess). The cases were drawn from all over the civilized world.

In this connection it may be of interest to note that the mode of feeding as shown by the investigations of the Phipps Institute has litfle to do with the implantation of the tubercle bacillus in the human subject. Of 665 cases of tuberculosis in adults, 90.9% were breast fed in infancy and only 9.2% bottle fed. The peculiar features of tuberculosis in infancy are especially emphasized by a study of its pathologic anatomy.

A very striking peculiarity of the pathologic anatomy of tuberculosis in infancy and childhood is the preponderating involvement of the lymph nodes and especially those of the lungs. Weigert was first to point out this fact and I remember that Prudden never tired of demonstrating it at autopsy. They are involved in fully 80% to 90% of all cases of tuberculosis in infancy and childhood. Ghon found that in Vienna the autopsies on children from Escherich's clinic gave as high as 98% of frequency in the involvement of these glands. When involved a primary pulmonary focus could always be demonstrated (Escherich, Kuss, Albrecht). Some have contended (Kuss) that they could demonstrate in these cases a port of entry in the tracheal mucous membrane. Others (Albrecht) demonstrated to their satisfaction that this primary focus in the lung existed in the lymphoid bodies of the fibrillar connective tissue of the lung. It may be accepted apart from the above that in tuberculosis of the bronchial lymph nodes, the primary lesion is in the lungs (Baumgarten). The peripheral lymph nodes are less often affected though in diseases of the pleura and apices of the lung the supraclavicular nodes may be involved and palpable (Finkelstein).

Primary tuberculosis of the tonsil is rare in infancy and childhood. Of 32 cases of tuberculosis of the tonsil Geipel proved that the primary infection was in all probability to be found in the lung in 13. I have published one case without autopsy in which the involvement of tonsil was the first *clinical* evidence of the tuberculous process in an infant, but I admit that in this case autopsy might have revealed a primary focus in the lung. The infant had been in the vicinity of phthisical people for some time.

Meningitis which is a general miliary tuberculosis, and is of great frequency in infancy and childhood, is peculiar to this period of life and of preponderating frequency as compared to the adult forms of tuberculosis. It is a hæmatogenous infection in most cases. Tuberculosis of the pericardium is rare and that of the larynx and trachea is always secondary.

The great infrequency of cavities[4] in the lungs of children as compared to that of the adult has been remarked upon especially by Hamburger and von Behring. In infancy Hamburger explains this by the fact that as in the experiment the guinea pig who has been repeatedly infected with a weakened virus may develop cavities in the lung, so the adult shows this tendency to cavity formation because his phthisis develops on a soil previously infected in infancy and childhood. The main reason, however, clinically is that in the infant and child infected up to the sixth year tuberculosis may and does run a rapidly acute course, thus allowing for cavity formation only in cases of slower course later in childhood.

[4] Cavities are not so infrequent in infants, and according to Aronade, Geipel found them in 8 of 30 cases, Finkelstein in 40% of his cases and Hohlfeld and Querin met them but rarely in the upper lobes of the lungs.

Clinical Features.

The clinical features of the various forms of tuberculosis in infancy and childhood are characteristic of this period of life and some of the forms are peculiar to infancy and childhood. The course of the tuberculous process under the fifth year of life is acute and even in the pulmonary cases the duration of the illness is quite short as compared to the chronic course of the disease prevalent in the adult. In the nursing infant the symptoms are often obscure and become evident only in the terminal stage of the disease. The initial period of the disease may run its course without fever. An obscure febrile movement with a temperature ½ to 1 or more degrees daily above the normal for weeks or months is quite characteristic of some forms of tuberculosis in infancy and childhood. I have recently seen a case of a boy of seven years of age who for years suffered from tuberculous adenitis, having been operated upon twice, who ran a low temperature of a degree or a degree and one-half above the normal for two years after operation.

I have for the purposes of this paper collected all the cases of tuberculosis coming to my hospital service in the past five years. Those before 1907 were only tested with the tests prevalent at the time. Others have been carefully confirmed both at the bedside and in the laboratory so that it is hoped a quite accurate résumé of the cases is given.

There were 209 cases in five years, dividing themselves as follows:

Tuberculous meningitis	158 cases.
Tuberculous pleurisies	23 cases.
Tuberculosis of the lungs	17 cases.
Tuberculosis of the peritoneum	8 cases.
Tuberculosis of other organs	3 cases.

It is not the intention of this address to take up anything but the broad features of the various forms and manifestations of tuberculosis, and, for this reason, when we consider sets of cases I shall limit myself only to striking features in the course of the disease.

It is first noticeable that the meningitic form of the disease is, *per se*, the one most looked for at the bedside. Of the total of all my cases, 75% took this form, bearing out in this respect the acute nature of the disease, the miliary form. It must not be forgotten that a large number of cases of meningitis are really terminal manifestations of a focus of tuberculosis long dormant. The history of this disease in many children bears

out this assertion. I have only to recall that in many cases of bone tuberculosis meningitis is the terminal stage of the disease. It is only in very early infancy and childhood that we see the disease burst forth after a preliminary short illness. Of my cases of meningitis fully 122, or 80%, occurred in infants and children below the fifth year of life. I had two infants stricken with the disease at the age of four months and one at 13 weeks. Some authors might be prone to trace the infection in such cases either close to the period of birth or even before it. Such is only speculation. There were 22 cases during the first year of life of the total of 158 cases, 14%. In many of these cases I could trace, in the history, the infection to the immediate vicinity or family of the patient. What a commentary on modern prophylaxis and what a sad lesson to parents should they for a moment understand the true state of affairs. Thus below the fifth year of life the most frequent form of tuberculosis is the miliary or, *per se*, the meningitic form. Later in childhood the miliary form of tuberculosis causes great uncertainty at the bedside. I cannot forget the cases of obscure fever which range from 103° to 105° F. to the normal with clear sensorium, with an apparent previous history of freedom from disease. In these cases the temperature range extended over two or more weeks with a negative von Pirquet reaction until the clear sensorium gradually became clouded and the patient passed into sopor and insensibility with all the signs of meningitis. Such cases cannot, because of the absolute absence of lung signs, except in the terminal stage, be differentiated from other forms of continued fever such as typhoid fever. The question of differentiation between typhoid fever and acute miliary tuberculosis is always a difficult one in later childhood, the fifth to eighth year. Not only the von Pirquet but also the Widal reaction fails us in many of these cases.

A study of my cases of tuberculosis of the lungs in infancy and childhood shows that here also the disease often runs an acute course. The physical signs at first simulate an ordinary broncho-pneumonia. The temperature, however, is continuous past the period of an acute broncho-pneumonia. The signs localized in most of my cases to the apices of the lungs on one or both sides, persist, fail to resolve, the emaciation, the failure of circulation (cyanosis) will raise suspicion at once of the tuberculous nature of the disease. If added to this there is a cough of a rasping, metallic nature and so-called expiratory dyspnœa, our doubt develops into certainty. Many of the pulmonary cases show glandular involvement in the form of enlarged supra-clavicular lymph nodes. Others show a stubborn diarrhœa. Many cases, especially those in later childhood, run a chronic course very much the same as in the adult. Hæmoptysis is not as frequent as in the adult. I have not met it in infants but have seen it in later childhood and then it was a precursor of rapid spread of the disease. The acute miliary form of lung tuberculosis occurs not only in infancy but in later childhood. I still cannot divest myself of the influence of the teachings of my master Henoch when I hestitate to diagnose clinically enlarged bronchial glands which, even with the X-ray, seem very difficult of diagnosis. It is true that in fully 80% to 90% of autopsies there is an enlargement of the bronchial lymph nodes but their diagnosis at the bedside, in spite of the teachings of the Vienna school, must be made with great caution. It looks too much like a forced attempt at making a pathological entity fit a clinical picture. Of the 17 cases of pulmonary tuberculosis all were below the age of three years, thus accounting for the acuity of the progress of the disease.

To me as a clinician the greatest interest centers in the cases of dry pleurisy and pleurisy with effusion which we meet in children who have not presented any symptoms of a previous pulmonary affection. What proportion of these cases are tuberculous? This is not only an important question but one which in practice brings us face to face with the necessity of action in regard to the future well-being of the patient. What kind of pleurisy is really of tuberculous nature in children? This question is best answered by looking over carefully sifted material of my hospital and private practice. In my hospital service during the past five years there have occurred 45 pleurisies. Twenty-three of these (50%) were manifestly tuberculous, sixteen were metapneumonic, seven occurred in subjects suffering from rheumatism and heart disease, and one in a nephritic. These statistics exclude all cases in which the effusion was not clear and serous macroscopically. As to age in the tuberculous cases 7 were below the age of 5 years, the remaining 16 ranged up to the 13th year. I think we may regard a pleurisy as tuberculous whose onset is not stormy though it may be acute or sub-acute, in which the temperature is not very high, 102°, 103° or even 104° F., in which the effusion is clear and absolutely free from organisms, in which there is a loss of flesh and strength and in which there is a history of tuberculosis in the vicinity of the patient, and in which there is a positive result to the tuberculin tests, either of the skin or subcutaneously. From this it will be seen that by no means can I regard the assertion of some (Hamburger) as true that almost all pleurisies in childhood, especially those with serous pleurisies between the ages of 2 or 3 years, are tuberculous.

We have found many metapneumonic pleurisies at this age with serous exudation in which there was a distinct preceding history of broncho-pneumonia and in which the exudate showed microorganisms. I think my figure of 50% of frequency of tuberculous pleurisies in infancy and childhood will be found nearer the truth.

In those cases of tuberculous pleurisy in which a blood count was made and in which a positive tuberculin reaction either of the skin or subcutaneously was obtained there are the following features.

The number of white blood cells in sixteen tuberculous cases ranged from 1100 to 20,000 to the cubic millimeter and the polynuclear leucocytes from 51% to 85% so that this gives us but little to serve as a guide.

More interesting is the cytology of the fluids obtained from the chest. In those cases in which such an examination was

made or was possible the lymphocytic nature of the cells in the fluid was quite apparent, in the tuberculous cases the lymphocytes ranged from 90% to 100%, this in the absence of any bacteria seems to me worthy of note.

In all the above I have absolutely disregarded all pleurisies which have suggested purulent exudate and only considered those in which the effusion was clear.

I have recently seen two cases in older children with a dry pleurisy extending over weeks not giving any symptoms but a mild hacking cough and still refusing to react to tuberculin. Such cases, I think, can well be traced to influenza or preceding broncho-pneumonia.

The importance of a definite decision in these cases cannot be overestimated as a pronouncement of tuberculosis means the breaking up of home or business, even among those of moderate means.

In discussing tuberculous peritonitis, I wish first to call your attention to the remarks of Heubner on intestinal tuberculosis in which he makes note of some of his cases occurring in infancy as also of tuberculosis of the mesenteric glands.[1] I have rather preferred to give a résumé of those cases in which the prominent symptoms were those of a tuberculous peritonitis. Of eleven cases, six presented complications in the lung, some cases were the miliary form, others the kind in which the formation of masses in the abdomen prevailed. The youngest case was twenty-two months of age; the older children ranged from ten to twelve years. I have seen a baby in private practice 4½ months of age with tuberculous peritonitis. It is my impression that the peritonitic form is not as frequently met with as other forms of tuberculosis in infancy and childhood.

I wish to call your attention and engage your interest in the remaining forms of tuberculosis. I refer to the form which for eras in medicine has been the source of much contention and discussion—this is the so-called scrofulosis. Some pediatrists who wish to be in the van of progress have, I think, prematurely suggested striking the word scrofulosis from our nomenclature. Lænnec was the one who first rescued the term from opprobrium and established the connection with tuberculosis of the glandular form of scrofulosis for all time. It is interesting to see the tenacity with which some of the great minds in pediatrics have clung to the idea that all scrofulosis is not tuberculous though they admit that scrofulosis may become tuberculous (Henoch). It would scarcely interest you to recite all the various authorities, Henoch, Heubner, Cornet, Escherich, Czerny, who have taken part in the discussion of what really constitutes scrofulosis. Allow me to say that with recent advances in our methods of diagnosis, we are fast beginning to recognize that in the term scrofulosis there is a distinct clinical tuberculous entity. I think for my part that the picture is so definite that it would be a pity to discard it, especially as it is a syndrome definitely peculiar to infancy and childhood. Escherich who has given this form of tuberculosis much thought comes to the conclusion that scrofulosis is a form of infantile tuberculosis which develops on the foundation of a lymphatic constitution. What is a lymphatic constitution? may be asked. It may be characterized as a tendency from earliest infancy to a hyperplasia of adenoid tissues in the body, *adenoides Gewebe*. These lymphatic children show enlarged tonsils, adenoids in the retronasal and pharyngeal space, enlarged lymph nodes throughout the body, and hyperplasia of the mucous membranes. Even in the intestines there may be an enormous hyperplasia of the solitary follicles in the whole extent of the small and large gut. The thymus gland is enlarged. Such children are anæmic and of a pasty complexion, they suffer from catarrhs of the mucous membranes and in many of them we have cyclic albuminuria. If upon such a soil there is implanted an infection with tubercle bacilli we have an especial vulnerability and over sensitiveness to external traumatism and the development of an allergie against minimal doses of tuberculotoxin. We have as a result, the development of skin eruptions in the form of scrofulides or tuberculides and later through the lymph and blood the formation of localized tuberculous foci or generalized tuberculosis. The clinical picture of scrofulosis is quite characteristic: the glandular enlargements in the form of tuberculous adenitis, catarrhal states of the conjunctivæ, the nose and respiratory tract, the affections of the bones, spina ventosa, osteomyelitis of the long and flat bones, including those of the skull, manifestations on the skin in the form of lupoid eruptions, ecthyma, tuberculides and scrofulides, and all affections of the various structures of the cornea and lens of the eye. All these focal inflammations do not always lead to death; they are slow to develop and tend to break down (glands) and suppurate, calling to their aid the mixed infections; they have a tendency to heal. Here is a distinct set of syndromes not seen in adult life. Occasionally we see isolated forms of the above inflammations in one patient. It is not uncommon to meet a tuberculous adenitis in an otherwise healthy looking child, or the tuberculous gland at the angle of the jaw may be combined with enlarged tonsils. Again an eye affection may for a time be the only focus apparent, or a hidden focus in a bone, as, for example, in the head of the tibia may be the only symptom in the patient, and then apparent only by the X-ray. As a rule, however, the typical scrofulous child is anæmic though well nourished; there are catarrhs of the conjunctivæ and nose, with enlarged glands about the neck, and the skin, as stated, shows eczematous tendency with or without tuberculides or ecthymata. In two infants recently under my care there were foci in the lung. I am inclined to believe that this is certainly a definite entity, and if I may theorize as others have, it is the result of repeated infections with minimal amounts of tubercle bacilli,

[1] There is a great discrepancy in the statistics of various investigators as to the frequency of primary intestinal tuberculosis.

Some put it at 0.9% of all tuberculous children (Baginsky) others as high as 47.6% (Edens) and some even at 16 to 20% (Beitzke).

In England Price Jones places the frequency of tuberculosis of the alimentary tract as high at 25% of all the cases of tuberculosis in children.

so that there is developed an active immunity against rapid advance of the disease. It may be as Escherich says that such a form of tuberculosis presupposes a lymphatic soil. At all events scrofulosis is an interesting entity, and I am not at all prepared to part with the term. It is in short the lymphatic form of tuberculosis.

The Diagnosis.

In the vast number of cases there is no difficulty outside of clinical perspicacity in surmising the diagnosis of tuberculous processes in infancy and childhood. The great advances in aids to diagnostic precision in the past ten years can only be appreciated by a study of the writings of a past decade and those of to-day. The uncertainty which at times is reflected in the writings of the master mind, Henoch, is not found in the works of the writer of to-day. This change has been made possible through a simplification of our ideas on the unity of the various pathological forms of tuberculosis not only confirmed at the autopsy table but in the bacteriological experimental laboratory. In the various forms of meningitis there are few difficulties in certain classes of cases. It is in the early stages of tuberculous meningitis that difficulties arise. I have recently pointed out that the differentiation of forms of encephalitis from those of meningitis gives rise to great and at times insurmountable obstacles.[6] In these cases the tuberculin reactions leave us if positive, in doubt; if negative, they are of value, and yet, as in other diseases the whole picture clears up as the disease progresses. Tuberculin reactions must be interpreted in light of clinical symptoms. The simplicity in the technique of tuberculin reactions has been due to the era-making work of Escherich, von Pirquet and their pupils, of the Vienna school. It has been shown simply by means of harmless technique that tuberculosis is one of the most prevalent of diseases among infants and children. At the same time it has also brought us more and more power over the remedy tuberculin than ever before. If some methods of using tuberculin such as the *Stich* reaction of Epstein, Escherich and Hamburger, and the cutaneous reaction of von Pirquet are harmless, especially the latter, we have learnt the dangers of other methods such as the ophthalmo-reaction of Wolff-Eissner. In the clinic, at the bedside, the mode of using tuberculin by preference is that of von Pirquet. If this leaves us in doubt we may make use of the *Stich* method of Hamburger. In this last method caution must be exercised until we become acquainted with the smallest dose of a tuberculin solution (O. T.)[7] beginning with 1/10 of a milligram and increasing the dose gradually up to 1/4 milligram which will be borne by the patient. I rarely pass beyond this. I will not here dilate on the peculiarities of the negative reactions, or so-called late reactions (*spät Reactionen*). This can be found in the writings of von Pirquet to which we cannot add anything, so classic have been the observations. I wish, however, to call attention to the negative reactions in the later stages of meningitis and lung tuberculosis, and also advanced miliary tuberculosis of the body and peritoneum which we have had abundant opportunity to confirm. In the cases of so-called scrofulosis the reaction and induration is in some cases simply enormous. The induration persists for a long time. The allergie in these cases is certainly exceptional, and is awake to an infinitesimal amount of tuberculotoxin proving that here we have a condition *per se* characteristic. Escherich called attention to this in these cases. In other words there was an increased immunity. Escherich explained also the skin eczema and lesions seen in these subjects on the theory that the secretions of these patients contained the tuberculotoxin, and when a scratch or wound of the skin was exposed to the action of the secretions of the patient a species of autoinoculation took place, an allergie was immediately manifest; hence, the recurrent inflammation of the skin in scrofulous patients.

I wish to call attention to a phenomenon which must have been evident to others. In tuberculous pleurisy of children, in whom a von Pirquet test has been performed, and a positive result obtained, it is well not to try the subcutaneous method of diagnosis, for the confirmation of the local nature of the tuberculosis, unless we are prepared for a recrudescence of symptoms. In two cases of pleurisy with effusion in whom a positive result was obtained by the von Pirquet method, I injected tuberculin to see first whether I could obtain a *Stich* reaction and whether there would be a rise of temperature. I obtained both but with them an increase in the fluid which had begun to absorb and an exacerbation of the local subjective and objective signs. In both cases the results were disquieting, especially as I regard the course of such pleurisies in children, even if tuberculous, as benign and with a tendency to spontaneous resolution, so that the recrudescence of symptoms in these cases seemed to be a warning not to persist in

[6] I wish to emphasize the fact that in tuberculous meningitis the careful study of the fluid obtained by lumbar puncture is of the highest importance. In the second edition of my treatise on the Diseases of Infancy and Childhood, 1906, and also in the third edition, I laid especial stress on the cytology of this fluid which showed a predominance of mononuclear cells.

In one case there was an equal number of mononuclear and polynuclear cells. The predominance of mononuclear cells is so constant in this disease as to be a characteristic, but not absolutely pathognomonic, element in the fluid obtained by puncture in cases of tuberculous meningitis apart from the presence of tubercle bacilli. In 13 of 14 successive cases clinically diagnosed as tuberculous meningitis in my wards Bernstein (Koplik, second edition, 1906) found tubercle bacilli in 13.

In the years 1904 to 1906, 29 cases diagnosed as tuberculous meningitis revealed tubercle bacilli in the fluid of puncture in 24. In two of these 29 cases a diagnosis was not fixed positively at the time of puncture. Thus in 24 of 27 cases punctured, tubercle bacilli were found as confirming the clinical diagnosis.

In some cases the bacilli were found only after death and I think this success was due to sedimentation post mortem of bacilli in the lower portion of the spinal canal.

These facts have convinced me that in all cases if the search were painstaking the bacilli could be found.

Holt recently, in a paper on meningitis, has confirmed this constancy of bacilli in tuberculous cases through his assistant, Dr. Hemingway.

[7] Old tuberculin.

this line of study. I record it here as a guide to others. I have never seen harm result from the cautious use of tuberculin, as I have sketched it in the diagnostic field. I do not nor does any one that I know of regard the reaction *per se* as diagnostic of the tuberculous nature of any focus, but rather simply that there is a tuberculous focus somewhere in the body though the lesion we may be studying at the time may have little to do with causing the reaction. This is well understood and we meet many cases in practice which illustrate this, and yet there are many physicians who cannot understand this simple fact. The simple presence of tubercle bacilli in an organ without the formation of tubercle tissue will not cause any reaction to tuberculin. This also is not generally understood by the practicing physician.*

I cannot close this paper without a reference to a mode of diagnosis which has recently come into clinical use in children with tuberculosis, and that is the X-ray. The X-ray is useful especially in localized bone tuberculosis to fix the location of a focus of disease. It is of value in other forms of tuberculosis, such as meningitis or lung tuberculosis for the demonstration of enlarged mediastinal glands or miliary foci in the lungs. I have recently studied cases of tuberculous meningitis with a view to detecting enlarged bronchial lymph nodes. It was possible to demonstrate the presence of enlarged lymph nodes during life at the root of the lungs, and of miliary foci in the lungs with frequent regularity in cases of meningitis and pulmonary tuberculosis in infants and young children. I cannot say that such Roentgen pictures are of great practical utility until the normal conditions about the root of the lung in infants and children shall have been studied both by the X-ray and autopsy.

*Tubercle bacilli are found most frequently in cases with formation of cavities in the lungs and cheesy pneumonia and then are seen in the sputum. The method of examining the sputum described by Holt is here noted but I have not been very successful in carrying it out.

I have found bacilli in the stomach contents and feces especially in advanced pulmonary and peritoneal cases.

Prognosis.

The prognosis of tuberculosis in infancy and early childhood is bad on account of the tendency of the infection at this time to spread and become general. The acute course of fully 75% of the cases has been emphasized in the statistics upon meningitis. The earliest ages at which a tendency of tuberculosis to cure has been observed are the cases of Schlossman and Aronade, 15 and 16 months, respectively. The older the child the better the prognosis. The best prognosis is beyond the age of seven years and I would say that the localized glandular and bone forms have a tendency to heal beyond this age limit.

Prophylaxis.

Much that is disputed ground can for a moment be omitted, and we are face to face with the fact that the greatest danger to the child lies in the vicinity and the surroundings of, the sufferer from tuberculosis. I doubt whether the average physician much less the layman realizes the sacrifice of infant life through the contact of children with tuberculous persons. As I have before intimated, children in the poor quarters of large cities and small ones for that matter are always among the grown-ups. They are the hapless playthings of the old decrepit cougher and the young unsuspecting tuberculous mother. The intimate contact with the mother or father who may be phthisical is at once apparent. It is not uncommon, even in public prints of welfare agitators, to find whole families who are tuberculous. Again vendors of candies and cookies are seen who on the surface are sufferers from tuberculosis. Added to this the universal habit among the poor of expectoration raises the chances of infection among the children. In the face of all this it seems far fetched to ascribe any marked influence in the causation of tuberculosis among children to milk from infected cows.

The future will lie very much in the direction pointed out by Grancher in France; the separation of infants and children from the vicinity of infection, if necessary from parents or vice versa. This is the gigantic work to be done by the city and state boards of health in the future.

THE EFFECT OF THE PREVENTION OF LAKING ON THE CATALYTIC ACTIVITY OF THE BLOOD.

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In the course of a study concerning the influence of feeding potassium iodide on the catalytic activity of the rabbit's blood, some experiments were made to test the effect of this salt when added directly to blood. These experiments were made with the blood of a normal person. The method of determining the catalytic activity of the blood was that used in former experiments.[1] The amount of blood taken was very small, varying from about 0.03 to 0.04 cc. in the entire series of experiments. The different series of experiments are not always comparable with each other because of the varying amounts of blood used. The hydrogen peroxide was neutralized, its strength was approximately three per cent and in each case five cubic centimeters were used.

The arrangement of the experiments was as indicated below. The number of cubic centimeters of liberated oxygen was determined every fifteen seconds for two minutes in duplicate

[1] Strauss: Johns Hopkins Hosp. Bull., 1912, XXIII, 51.

experiments. The figures given are the averages of two well agreeing determinations at the end of one minute.

1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + H_2O_2.
3. 5.0 water + blood + 5.0 $\frac{m}{5}$ KI + H_2O_2.
4. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.

The number of cubic centimeters of oxygen liberated in sixty seconds was:

1	2	3	4
39.0	5.5	47.5	18.6

Subtracting the amount of oxygen liberated by the potassium iodide solution alone we have:

1.	3	4
39.0	42.0	13.1

It is seen that the potassium iodide solution itself liberates a certain amount of oxygen.[1] When this solution is added to blood which has been taken up in water first, more oxygen is liberated than by the blood alone. But when the blood is added last to a mixture of the potassium iodide solution and water, a very marked diminution of the liberated oxygen takes place. Under this condition the blood is not laked.

In the experiment with addition of the potassium iodide solution to the laked blood the amount of oxygen liberated exceeded somewhat the sum of oxygen liberated by the blood and by the potassium iodide itself. But in other experiments, a simple summation of the effect of blood and of potassium iodide was noted. The experiments were repeated with potassium iodide solutions of different concentrations, always with the result that this marked inhibition did not occur when the blood was laked. On the addition, however, of more concentrated solutions of potassium iodide, as, for instance, a $\frac{m}{25}$ solution, it was noted that after subtracting the oxygen liberated by the iodide solution itself a smaller amount of oxygen was obtained even when the blood was previously laked. Here the known influence of salt solutions on the catalytic activity of the blood becomes manifest, as it did in a number of experiments with solutions of sodium chloride.

For the purpose of this paper it is not necessary to record the results of all experiments with salt solutions of different concentrations. It will suffice to show that the prevention of the laking of the blood depresses its catalytic activity.

In the following tables the results of experiments are given where the blood was not laked, comparing the values with those obtained with blood laked in water without the addition of salt. In the case of the potassium iodide experiments the oxygen liberated by the iodide solution itself is subtracted.

[1] Concerning the mechanism of this reaction see Péchard: Compt. rend. Acad. d. sc., 1900, CXXX, 1705.

A. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.

1	2	3	4
39.0	13.1	11.2	12.6

B. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.
5. 5.0 water + 5.0 $\frac{m}{25}$ Na citrate + blood + H_2O_2, not laked.

1	2	3	4	5
27.0	8.9	8.2	8.2	7.8

C. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{25}$ Na citrate + blood + H_2O_2, not laked.

1	2	3	4
25.6	8.0	8.4	8.6

It is evident that the prevention of the laking of the blood reduces its catalytic activity and in this particular case very considerably. The fact that in these experiments the figures obtained are rather constant is very remarkable. For instance the number of cubic centimeters liberated on the addition of $\frac{m}{2}$ or $\frac{m}{5}$ NaCl shows only negligible variations, while the addition of the more concentrated salt solutions to the laked blood causes a very marked depression of its catalytic activity. For instance, taking examples from the series of experiments just referred to:

B. 1. 10.0 water + blood + H_2O_2 } laked.
2. 5.0 water + blood + 5.0 $\frac{m}{2}$ NaCl + H_2O_2 }
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 }

C. 1. 10.0 water + blood + H_2O_2 } laked.
2. 5.0 water + blood + 5.0 $\frac{m}{2}$ NaCl + H_2O_2 }
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 }

	1	2	3	4
B.	27.0	15.8	8.2	8.2
C.	25.6	14.0	8.0	8.4

The experiments reported thus far were made with the blood of the same individual. In the following experiments the blood of different healthy individuals was used. These experiments are comparable with each other but not with those previously given, because the amount of blood exceeded that used before. The arrangement of the experiments was the following:

1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
3. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 } not laked.

The Roman figures designate the different individuals.

	I	II	III	IV
1.	44.2	45.5	37.2	20.5
2.	15.4	15.5	12.9	11.9
3.	15.5	15.6	14.7	12.9

With exception of No. IV the ratio of the catalytic activity of the unlaked blood to that of the laked blood is approximately 1 : 3.

The blood of No. I was used for a series of experiments, in which the concentration of the salt solution was gradually diminished. The strength of a $\frac{m}{5}$ NaCl solution is approximately 1.2 per cent.

	Before addition of H_2O_2.	No. of cc. O_2 liberated in 1 minute.
10.0 1.00% NaCl + blood + H_2O_2	not laked	15.8
10.0 0.66% NaCl + blood + H_2O_2	not laked	16.4
10.0 0.60% NaCl + blood + H_2O_2	not laked	21.7
10.0 0.50% NaCl + blood + H_2O_2	laked.	43.1

There is a marked difference in the catalytic activity with the diminution of the salt concentration from 0.66 to 0.6%, although in both instances there was no apparent difference before the addition of the hydrogen peroxide, the blood not being laked. It is not unlikely that the addition of the five cubic centimeters hydrogen peroxide dilutes the salt solution in the latter case sufficiently to permit a slight laking.

The following experiments made with the blood of another individual support this view:

1. 10.0 water + blood + 5.0 H_2O_2.
2. 10.0 water + blood + 10.0 H_2O_2.
3. 10.0 1% NaCl + 5.0 H_2O_2.
4. 10.0 1% NaCl + 10.0 H_2O_2. } not laked before the addition of H_2O_2.

1	2	3	4
32.0	27.4	9.7	13.6

In Case No. 3, the concentration of the salt solution was reduced to 0.66% by the addition of the hydrogen peroxide, in Case No. 4, to 0.5%. It was found that this salt concentration was not sufficient to insure a complete laking of the blood. In Case No. 2, it is seen that the addition of larger amounts of hydrogen peroxide depresses the catalytic activity to a certain extent. In the following case the same results were obtained. The blood came from a different individual and the strength of the sodium chloride solution was 1.2%.

1	2	3	4
43.7	38.4	16.2	20.0

Here also it is to be noted that this blood did not lake completely with a concentration of sodium chloride of 0.6%.

In spite of the depressing influence of larger amounts of hydrogen peroxide the addition of 10 cc. instead of 5 cc. hydrogen peroxide increased the catalytic activity of the blood unlaked before the addition of the peroxide. This fact is most readily explained by the diminution of the salt concentration.

Therefore in studying the effect of the prevention of laking the blood on its catalytic activity the salt concentration must be such that the addition of the hydrogen peroxide does not reduce it to a hypotonic level.

In order to show the influence of the prevention of the laking of the blood in a different manner a few experiments were made where the blood otherwise unlaked in a $\frac{m}{10}$ sodium chloride solution was laked by the aid of ether.

It was found that the blood could be laked by adding ether to the solution of sodium chloride. The usual amount of blood was added to 5 cc. $\frac{m}{5}$ NaCl. On addition of 0.8 cc. ether the blood remained unlaked, but on adding 4.2 cc. water and shaking, laking took place. The arrangement of the experiments therefore was this:

1. 10.0 water + blood + 5.0 H_2O_2.
2. 5.0 $\frac{m}{5}$ NaCl + blood + 5.0 water + 5.0 H_2O_2, not laked.
3. 9.2 water + blood + 0.8 ether + 5.0 H_2O_2.
4. 5.0 $\frac{m}{5}$ NaCl + blood + 0.8 ether + 4.2 water + 5.0 H_2O_2, laked.
5. 5.0 $\frac{m}{5}$ NaCl + blood + 0.5 ether + 4.5 water + 5.0 H_2O_2, } not laked.

1	2	3	4	5
43.7	16.2	47.9	36.4	16.4

The figure given for experiment No. 4 is an average of four rather widely differing determinations, the single determinations giving 32.4, 34.2, 36.4 and 42.4 cc. oxygen. It is possible that the conditions of the experiment are such as to render a uniform laking less reliable. Nevertheless the results are sufficiently striking to show the discrepancy between the catalytic activity of laked and unlaked blood in salt solutions of the same concentration. The increase of the catalytic activity in No. 3, where ether was added to laked blood is not due to any catalytic activity of the ether employed, since a control with this ether alone did not liberate any oxygen. Neither is it likely that the hydrogen peroxide usually found in ether after standing can be responsible for this increase. It is to be noted that in No. 5, where the amount of ether added was insufficient to lake the blood, the catalytic activity was the same as in No. 2, where no ether had been added.

That the activity of No. 4 did not reach that of No. 3, in spite of the laking of the blood, agrees with other observations

where the catalytic activity of laked blood in a $\frac{m}{10}$ NaCl solution was determined. Here the blood was laked by first adding 5 cc. water and then 5 cc. $\frac{m}{5}$ NaCl. As a rule the catalytic activity of the blood under these conditions fell below that of blood laked in water without addition of salt. With the increase of the salt concentration to $\frac{m}{4}$ this inhibiting effect of the salt became much more pronounced as indicated in the foregoing.

The result of the experiments shows that the prevention of the laking of the blood depressed its catalytic activity. This depressing effect is not surprising, since the investigations of Bergengruen[1] have demonstrated that the power of the blood to decompose hydrogen peroxide resides chiefly in the body of the red blood corpuscles. An experiment with rabbit's blood showed us that the red blood corpuscles yield their catalase to distilled water, while the stromata of the corpuscles after extraction with water are practically inactive.

[1] Bergengruen: Ueber die Wechselwirkung zwischen Wasserstoffsuperoxyd und verschiedenen Protoplasmaformen. Inaugural Dissertation, Dorpat, 1888.

It is remarkable in our experiments that the salt solution of different concentrations depressed the catalytic activity to a rather constant level, provided the concentrations were sufficient to prevent laking. So the catalytic activity of a given blood was not depressed any further, at least not to a marked extent, when the determinations were carried out with a $\frac{m}{4}$ instead of with a $\frac{m}{10}$ NaCl solution; and this in spite of the fact that a $\frac{m}{4}$ solution depressed the catalytic activity of the laked blood very considerably more than a $\frac{m}{10}$ solution.

The possibility was considered whether the comparison of the catalytic activity of the laked and unlaked blood might be able to give us some information concerning the distribution of catalase in the blood, permitting a distinction between catalase contained in the red blood corpuscles and catalase occurring free in the plasma. It is more probable, however, that the explanation of our results lies in another direction, which at present cannot be stated definitely.

Conclusion.

The prevention of the laking of the blood depresses its catalytic activity.

PIN WORM APPENDICITIS.

By Grover C. Ney, M. D.,
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The occurrence of the oxyuris vermicularis within the appendix is comparatively a common occurrence, but recognized cases of appendicitis caused by this worm are very uncommon, and we therefore wish to report the following two cases which were operated upon at the Hebrew Hospital:

Case 1.—E. M., age 21 yrs., female, married. Admitted to the hospital on January 2, 1911, complaining of pain in her right side, localized at McBurney's point.

Family history: Negative.

Past history: Negative, except for the fact that patient has had some indigestion and is somewhat constipated. There is no history of a previous attack of pain in the region of the appendix.

Present illness: Patient began to have severe pains in her abdomen on December 28, 1910, associated with vomiting; these pains gradually became more severe and paroxysmal in character. Purgatives were administered but failed to relieve the suffering. On the date of admission the pains were so severe that the patient was compelled to have a sedative.

Physical examination: Abdomen negative except that extreme tenderness and some rigidity over the right iliac region are noted. A vaginal examination is negative except for the tenderness elicited on the right side; and a rectal examination is also negative. Urine negative. Temperature 98.4° F., pulse 105, respiration 25. The leucocyte count is 5000; and a differential count shows:

Polymorphonuclears	64
Small mononuclears	30
Large mononuclears	3.5
Transitionals	1.5
Eosinophiles	1

The stools show a considerable quantity of mucus and an occasional Trichomonas hominis. No pin worms were found. In spite of the various negative symptoms an immediate operation was decided upon.

Operation: The abdomen was opened by a right rectus incision and the appendix was found behind the cæcum, bound down by a small adhesion, which was liberated; the appendix was removed, and the stump invaginated. On examination the appendix looked fairly normal, except for a few markedly dilated blood-vessels. It was opened and five pin worms crawled out.

Pathological report: On macroscopical examination the appendix showed some adhesions but no other signs of inflammation. On microscopical examination there were evidences of a catarrhal inflammation of the mucosa, but the other coats were not involved. No eggs of the oxyuris were found upon the mucosa. The worms were active only for a few minutes after the appendix was opened and then died; all were females and filled with ova. Patient made an uninterrupted recovery and left the hospital on January 20, 1911, cured.

Case 2.—F. P., age 17 yrs., female, single. Admitted to the hospital on April 15, 1911, complaining of pain in her right side.

Family history: Negative.

Past history: Has had measles, whooping cough and influenza. Bowels very constipated, appetite good. Has been troubled with indigestion for some time. Has lost some weight in the last year. Gives no history of previous attacks of pain in her right side.

Present illness: About 5 a. m. on the 13th, the patient was seized with severe abdominal pain which finally localized itself on the right side. It continued and grew worse, being extremely severe in the evening. She then had a chill and vomited. On the fol-

lowing day she took calomel, but the pains continued and she finally decided to enter the hospital on the 15th.

Physical examination: Patient's whole appearance indicates that she is suffering a great deal. The examination is negative except for the abdomen, which is extremely tender to pressure over the right lower quadrant, and there is a slight rigidity of the muscles. The vaginal and rectal examinations are negative; the urine is negative. Temperature 99.2° F., pulse 92, respiration 20. The leucocyte count is 19,800.

Operation: Abdomen opened by McBurney incision. There were about 3 ozs. of clear fluid in the Douglas cul-de-sac. The appendix was easily located; there were no adhesions, no concretions and no kinks felt. It was removed and the stump invaginated. The appendix looked fairly normal, but on opening it two pin worms crawled out.

Pathological report: No signs of inflammation made out on macroscopic examination. On microscopic examination the inner layer of the appendix showed signs of catarrhal inflammation. The worms were females and filled with ova; no eggs were found upon the mucosa.

Patient made an uninterrupted recovery and left the hospital on June 8, 1911, cured.

Oxyuris vermicularis is the most common of intestinal parasites. Its ova are probably carried into the body by means of water or vegetables; they are elliptical, measuring from 59 to 72 by 40 to 50 microns, and have an envelope which is absorbed by the digestive juices, when the embryo is liberated within the small bowel. They occupy the intestinal tract from the jejunum to the rectum. These worms were formerly called "seat" worms, from the old idea that they especially inhabited the rectum, but this idea is erroneous. It is true that the females migrate to the rectum to lay their eggs; they slowly wriggle down the mucosa of the bowel to the anal margin, where the eggs are deposited. These worms have been demonstrated by O. Wagener to lie within the deeper layers of the bowel, and Osler has reported cases in which the worms have migrated to the Douglas cul-de-sac. The worms are small, rounded, and tapering at both extremities. Their ends are sharp and penetrating, by means of which they burrow their way into or through the various layers of the intestine. The female worm is much larger than the male worm, being 8 to 12 mm. in length, while the male is only 3 to 4 mm.

As early as 1534 Fabricius ab Aquapendente found a pin worm in the appendix, and Santorini in 1764 confirmed the above fact, and thought the chief function of the appendix was to serve as a nest for the round worm where it might be harbored and prevented from escaping into the general intestinal tract. As the cæcum is the common habitat of the pin worm, they readily crawl into the appendix to lay their eggs. It is possible that in certain cases they cannot escape, but the fact, however, that usually they easily escape does not indicate that they may not have been the prime cause of an attack of appendicitis. By means of their sharp ends they can easily burrow a hole into the mucous membrane; thus they produce a suitable entrance for the bacterial flora of the intestine and set up an inflammation within the non-resistant tissues of the appendix. In this manner a large number of cases of ordinary appendicitis in which worms have not been found could have been produced by the parasites, which had done their damage and then finally departed. If the worm should die within the appendix, the intestinal flora of bacteria acting upon the putrifying worm could also give rise to symptoms similar to the cases of appendicitis in which the lumen of the appendix contains nothing but a small quantity of fecal matter and no signs of inflammation.

There are three classes of cases of pin worm involvement of the appendix. Firstly, pin worms are found in the appendix without symptoms, especially in children. Secondly, there are cases where the worms are found in the appendix giving rise to acute appendicitis with no macroscopical evidence of inflammation, but on microscopical examination small areas of inflammation are found upon the mucosa. Thirdly, the cases with all the clinical symptoms of appendicitis, where the appendix shows macroscopical as well as microscopical areas of inflammation, and even gangrene or peritonitis may be present.

Symptoms: The symptoms of appendicitis due to pin worms vary somewhat from the symptoms of ordinary appendicitis. In our cases we were impressed with two—the extreme hyperæsthesia during the attack and the marked paroxysmal character of the pain. The attacks were agonizing, the patients cried out on the least pressure over McBurney's point. These two symptoms were entirely out of proportion to the degree of inflammation. In both cases we were surprised on opening the abdomen to find the appendices looking macroscopically almost normal. In our cases the attacks were the first attacks of appendicitis, but there are a number of cases reported in which the patients had as many as eight attacks before they were operated upon. The paroxysms last from two to forty-eight hours.

The character of these attacks may be accounted for as follows: these small worms bury their sharp ends into the appendiceal mucosa, which is followed by a peristaltic contraction of the appendix in its endeavor to expel the parasite, thus causing the agonizing colic.

The temperature and pulse in these cases have no particular bearing upon the diagnosis.

The leucocyte count varies and is of no diagnostic significance. The differential count is of no particular importance and the eosinophiles may or may not be increased.

The symptoms bear no relation to the number of worms; which may vary from one to one hundred, those with one or two causing as severe symptoms as those with a larger number. It is true that a large number of worms could lie in a conglomerate mass in the cæcal orifice and obstruct the appendix. This indeed would be an excellent environment to give rise to inflammation and suppuration.

Treatment: The treatment of all cases of pin worm appendicitis is appendectomy, no matter how mild the case. In looking over the literature we find that a large number of the patients have had recurrent attacks of appendicitis, colicky

in character, and some of these have had to be operated upon as emergency cases. Both gangrene and peritonitis have been found. This is probably due to the fact that in the primary attack only small areas of the mucosa are involved and after a number of such involvements the areas of inflammation increase until gangrene results.

In the last hundred cases of appendicitis in the Hebrew Hospital a careful examination of every appendix removed has revealed three cases of pin worms within the appendix.

In conclusion I wish to thank Dr. Randolph Winslow and Dr. St. Clair Spruill for the privilege of both operating upon and reporting these cases which occurred in their services.

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NOTES ON NEW BOOKS.

International Clinics. Vol. IV. Twenty-first Series. (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

The scope of these "Clinics" is gradually enlarging and we are glad to note in this volume two papers on the Economics of Medicine, an important subject to which the majority of the profession has given but little attention. There are other good articles on Treatment, Diagnosis, Medicine, Surgery, Otology, Pædiatrics, Opthalmology, Legal Medicine, the History of Medicine, and Geriatrics—a word quite unfamiliar to most readers, signifying the treatment of diseases of old age. The "Clinics," with their international character as contributions from European and American physicians, offer much of practical value to the general practitioner.

E. Merck's Annual Report of Recent Advances in Pharmaceutical Chemistry and Therapeutics. 1910. Volume XXIV. Darmstadt, July, 1911. (*New York: Merck & Co.*)

There is much that is of value in these reports, for they are carefully prepared in abstract form from the medical literature of all countries, and those interested in pharmacology and therapeutics will frequently find occasion to refer to them. The contents of this well printed, paper-bound volume are as follows: The Cacodylates and their Therapeutic Uses, Kephir, Preparations and Drugs, Bibliographical Index, Index of Authors, General Index, and Index of Diseases, Symptoms and Indications for Treatment.

Spirochætes: A Review of Recent Work with Some Original Observations. By W. CECIL BOSANQUET, M. A., M. D., etc. Illustrated. $2.50. (*Philadelphia and London: W. B. Saunders Co., 1911.*)

The author finding himself in possession of an enormous number of abstracts as a result of the necessity of a careful search through the literature on spirochætæ, thought it advisable to use these abstracts in the preparation of a book which would serve as a collective review on the subject.

He has attempted to locate the spirochætæ in their proper place in the scale of living things and feels inclined to consider them as more closely allied to the bacteria than to the protozoa.

The statements of various writers on the morphology and other characteristics of spirochætæ have been correlated with a view of establishing the features of the genus. In the latter part of the book the separate species have been described in some detail. A very valuable bibliography has been appended.

Containing, as it does, a description of all these various organisms, together with details concerning the best methods to be employed in studying them, the book constitutes a distinct addition to any reference library. It fulfils the object of its author and is an excellent review on the subject. L. G. R.

Hints for the General Practitioner in Rhinology and Laryngology. By DR. JOHANN FEIN. Translated by J. BOWRING HOGAN, M. B., etc. Illustrated. (*New York: Rebman Company.*)

In the preface, written by the translator, he apologizes for being instrumental in introducing "yet another small book upon the subjects of rhinology and laryngology." This book, however, is an exception; it is far superior to the average compendium in that it is not merely a collection of abstracts from the various textbooks, but consists almost entirely of the personal observations and experiences of the author.

Most of the common lesions of the nose and throat are mentioned, together with some valuable suggestions concerning the local appearance, the various methods which may be used in making a diagnosis, and the treatment of each condition. The book is well worth reading and is, in many ways, an improvement upon works of a similar kind and size.

Report of the Surgeon-General, U. S. Army. To the Secretary of War, 1911. (*Washington: Government Printing Office, 1911.*)

There are several important points brought out in this report, which it is of interest to note. Perhaps the most striking is the proven value of antityphoid vaccinations, which have now been practiced on a large body of men with brilliant results. This is a means of prevention which seems almost, if not quite, as good as vaccination against smallpox, and it is most necessary that the laity should be taught its value, so that in all our larger cities where typhoid prevails annually, the people should make use of this harmless means of guarding against a serious illness when they are exposed to it.

The prevalence of alcoholism and venereal diseases go hand in hand, and those interested in the welfare of our soldiers should strive hard to secure reforms in our barracks. Existing conditions in army life favor these evils, and the proposed remedy of cutting off the soldier's pay when ill from these diseases does not seem an altogether just one, unless means are taken to make his life more endurable at the army posts. If any such remedy is approved by the authorities it should apply to all men in the army, no matter what their rank.

There is a striking table (p. 81) showing "influence of season, United States (excluding Alaska), year 1910," upon the health of the enlisted men. The prevailing diseases, exclusive of venereal diseases, which brought the soldiers into the hospitals or rendered them temporarily non-effective, were during the months of Janu-

ary to June, inclusive, and October, November and December, tonsillitis and acute bronchitis; from July to October, diarrhœa and enteritis. This would at least seem to indicate the necessity of careful examination of the throats of all recruits as well as enlisted men, and the eradication of diseased tonsils, and also a careful study of the diet of the men during the summer months.

Many other points are well worth commenting upon and careful consideration, but those interested in these medical problems will secure the report for themselves, and a thorough study of it will repay them.

The health of the army, on the whole, is most satisfactory, and the work of the army medical officer deserves the highest praise. There is steady improvement all along the line, and we may well feel proud of the medical service in the United States Army.

BOOKS RECEIVED.

Electricity. Its Medical and Surgical Applications, including Radiotherapy and Phototherapy. By Charles S. Potts, M. D. With a Section on Electrophysics, by Horace Clark Richards, Ph. D., and a Section on X-Rays, by Henry K. Pancoast, M. D. With 356 illustrations and 6 plates. 1911. 8vo. 509 pages. Lea & Febiger, Philadelphia and New York.

A Handbook of Medical Diagnosis. In Four Parts. I. Medical Diagnosis in General. II. The Methods and their Immediate Results. III. Symptoms and Signs. IV. The Clinical Applications. By J. C. Wilson, A. M., M. D. 418 text illustrations and 14 full page plates. Third edition, thoroughly revised. [1911.] 8vo. 1438 pages. J. B. Lippincott Company, Philadelphia and London.

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A Manual of Fevers. By Claude Buchanan Ker, M. D. (Ed.), F. R. C. P. (Ed.). 1911. 12°. 314 pages.

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Clinical Diagnosis. A Text-Book of Clinical Microscopy and Clinical Chemistry. By Charles Phillips Emerson, A. B., M. D. Third edition. 1911. 8vo. 724 pages. J. B. Lippincott Company, Philadelphia and New York.

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